Remember the Time and Place for the Meeting of the American Pharmaceutical Association—Hotel Adolphus, Dallas, Texas, August 24th–29th. Rates and Routes, See Report Committee on Transportation.

AUG 10 1936

Vol. XXV, No. 7 JULY, 1936

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 84th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN DALLAS, TEXAS, AUGUST 24–29, 1936. Hotel Adolphus, Headquarters.

Local Secretary, Walter D. Adams, Forney, Texas.

The 1936 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Dallas, Texas.

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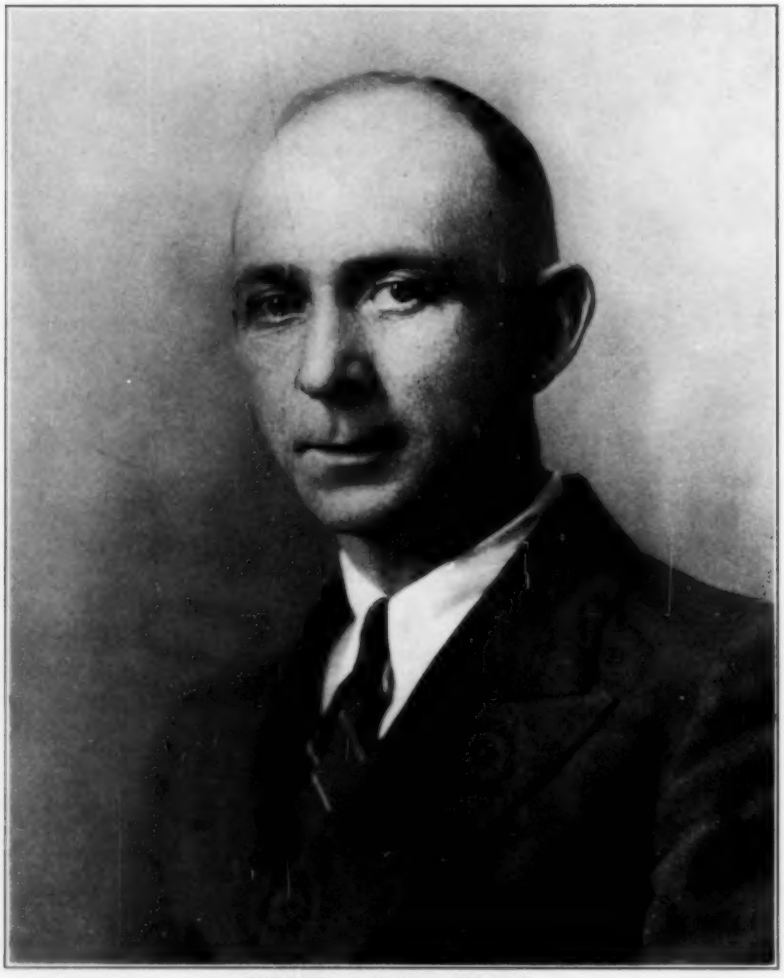


WESLEY McCLUNG CHILDS.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXV JULY, 1936 No. 7

THE PRESIDENT OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY.

Wesley McClung Childs, "Mac," president of the National Association of Boards of Pharmacy, was born at Columbus, Kans., November 13, 1895. He received his early education in the grade and high school of Kansas City, Kans. Thereafter, he graduated from the Pharmacy School of the University of Kansas. He was a student at the University of Montpellier, Herault, France, and earned the degree of Ph.C.

Mr. Childs enlisted on the day the United States entered the World War (1917) and went overseas as sergeant of Ambulance Company No. 139, 35th Division; he was later transferred and assigned as chemist in charge of Water Analysis for combat troops. While with the American Expeditionary Forces, in France, he participated in the engagements at Thann, St. Mihiel, Argonne Forest, Gerardmier, Dieu-Sommedieu. After two years of service Mr. Childs received honorable discharge at Camp Funston, May 1, 1919. Every male member of the family served overseas in the trenches; the father, W. R. Childs, was badly gassed and shell-shocked and a brother, Joseph, was killed in service.

The subject of this brief sketch has owned and operated The Hospital Pharmacy, El Dorado, Kans. for 17 years, and the Childs Manufacturing Company for the past 8 years; the latter establishment manufactures the Childs Prescription File and other pharmaceutical equipment.

Mr. Childs is a former president of Kansas Board of Pharmacy and is its secretary; he has held important offices in the National Association, as former vice-president, and is now its president. He was president of the Kansas Pharmaceutical Association in 1933, has held the office of secretary, is a member of the executive committee, served as chairman of the legislative committee of both state and national organizations and has been one of the leading and influential personal forces in Kansas pharmacy for a number of years.

President Childs is a member of the AMERICAN PHARMACEUTICAL ASSOCIATION, of the National Association of Retail Druggists, of the Kiwanis Club, of the American Legion, Veterans of Foreign Wars, and is a member of the Masonic bodies.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

THE PROGRESS OF PHARMACY.

WE HAVE come a long way since 1852. A mark of the progress of time is noted by the number of state associations which have concluded fifty years of organized effort with golden anniversary celebrations. We have every right to be proud of the record of the AMERICAN PHARMACEUTICAL ASSOCIATION in promoting the interests of the profession during the eighty-four years of its existence.

Profound changes in our economic and social structure have occurred during this period, but we are more aware of the progress and advances in the art and science of pharmaceutical practice since its beginning. We can be proud of the fact that all of the credit for the development of our science belongs to the profession itself. The AMERICAN PHARMACEUTICAL ASSOCIATION deserves much credit for its influence and direction. What seems most remarkable about it all is the fact that, eighty-four years ago, the men who recognized and asserted the needs of Pharmacy were able to act as wisely as they did and lay a foundation of which a large part still stands.

Public health service, service to the physician and the public, has been and will always be the first order of the pharmacist. Interprofessional relations between the physician, dentist and pharmacist have been evident during the years. The same reasons which early prompted that small group of professionally minded pharmacists to band themselves together should prompt us to meet the more pronounced needs of to-day when the pace of progress is more rapid. The movement to create a greater spirit of coöperation between physicians, dentists and pharmacists is taking a definite form. Pharmacists should welcome the opportunity to coöperate to the fullest extent with others interested in public health. It is reassuring to see evidenced a greater interest in pharmacy by pharmacists and a greater recognition of both by the allied public health groups and the public.

Pharmacy is well equipped to meet the demands upon it and will either succeed in doing so or fail, depending upon the influence and direction applied. The AMERICAN PHARMACEUTICAL ASSOCIATION must continue to assume the responsibility of leadership.

This responsibility cannot and will not be ignored by the ASSOCIATION nor its officers. Through coöperation, understanding and the individual effort of our membership Pharmacy will assume its proper rôle.—P. H. COSTELLO.

THE FEDERAL FOOD AND DRUGS ACT.

THERE was an evident desire or willingness on the part of the drug trade activities to have new food and drug legislation enacted. There were differences among organizations affected, but these differences were not the immediate cause for the failure of the enactment. Either revision of the present Act or new legislation as submitted, *i. e.*, with certain changes, seemed necessary, but the lateness of the session and differences of opinion relative to phases of control in administration bodies and among the members of Congress, prevented acceptance of the conference action. The House insisted on its provision giving the Federal Trade Commission jurisdiction over advertising of foods, drugs and cosmetics; Senator Copeland "would not deprive the Food and Drug Administration of essential control over matters pertaining to public health."

The result points out that in measures of this kind there is a possibility to bring about an understanding which will serve the public better than a misunderstanding, if there is a willingness to reach conclusions that are uninfluenced by the sources of motives, but it is difficult to accomplish agreement in a last minute consideration.

It may be questioned whether a new law is necessary or whether shaping of present legislation is better, but legislation of this kind is for the protection of public health; it is a means that requires careful consideration, fairness in framing and in defining effective standards.

There were many changes in the bill, not much to criticize; perhaps the outstanding criticism to offer was that action was too long delayed and then hurried action expected on a very important measure. There may not have been jealousies, but there were contentions which prevented revision or enactment of the food and drugs law.

When the subject comes up again there should be early rational discussion without unwarranted disparagement, with a purpose to bring legislation into form which will have public health service as a first and paramount aim.

COMMISSIONED RANK FOR PHARMACISTS.

PHARMACISTS have had professional rank for several years under the Civil Service and commissions in the Public Health Service. During the 2nd session of the 74th Congress the National Defense Act relating to the Medical Administrative Corps was amended to provide commissions for pharmacists who are graduates of recognized schools or colleges of pharmacy, requiring four years of instruction for graduation, under such regulations as the Secretary of War shall prescribe. The President has signed the Act; this provides the basis, in the future, for the organization of a Pharmacy Corps when the number of commissioned pharmacists is increased; its adoption also makes possible the commissioning of pharmacists in the Reserve Corps and in the National Guard, as soon as arrangements can be worked out, which means that a properly organized pharmaceutical service can be established in time of War or of other necessity.

The AMERICAN PHARMACEUTICAL ASSOCIATION and affiliated organizations have contributed to the success of the enactment, and much credit is due to Surgeon General Charles R. Reynolds, who soon after his appointment gave attention to the question of improving the pharmaceutical service in the Medical Department of the Army and to giving pharmacists commissioned rank.

The bill (S. 4390) presented by Senator Morris Sheppard was amended in accordance with the views of the War Department and from that time forward the measure received the undivided support of the members of the Committee on Military Affairs of the Senate; of Representative John J. McSwain, Chairman of the House Committee on Military Affairs, of the members of the Committee; in fact, the bill did not receive an unfavorable comment or a negative vote in its passage through both Houses of Congress. The very evident purpose is to have pharmacy render an essential service, and the legislation contributes advancement to the profession.

The Medical Administrative Corps has an authorized strength of 72 officers; the bill limits future commissions in this Corps to pharmacists, and the 16 commissions at present authorized are estimated to cover the vacancies expected within the next year.

References to the measure and to those who were helpful in the promotion have been made in prior issues of the JOURNAL. The Acting Secretary of War, Harry H. Woodring, referring to enlisted men of the Medical Department with meager qualifications for such commissions, stated they have not materially added to the efficiency of the Medical Service because of their lack of professional and technical experience and attainments, and the letter from the War Department, bearing on the subject, closes with the statement that this legislation "will give these specialists the recognition in rank to which they are entitled."

Pharmacists will improve their opportunities and contribute to the professional service of pharmacy. The effort represents one of the promotions of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Parts of *Bulletin No. 15*, A. PH. A., of June 22nd, have been embodied in this comment.

THE PHARMACY EXHIBIT AT THE TEXAS CENTENNIAL.

ON PAGE 573 of this issue of the JOURNAL a view of the pharmacy exhibit at the Texas Centennial is shown. Chairman H. C. Christensen contributed largely to the success of the pharmacy exhibit at the Chicago World's Fair and Dr. Eben J. Carey, Chief of the Medical Section, Hall of Science, has donated to the AMERICAN PHARMACEUTICAL ASSOCIATION an illustrated volume, depicting the medical sciences. Plates 37–39 show the pharmacy exhibits and pages 70–74 describe them and give the history therewith. Coöperating with Mr. Christensen at Chicago were Miss Esther Barney and Mr. Thaddeus Niemic, who were in attendance and contributed largely to the interest of the visitors at this exhibit. These co-workers designed and installed the Texas Exhibit and they were present at the opening in Dallas on June 6th.

The AMERICAN PHARMACEUTICAL ASSOCIATION sponsored the latter, upon invitation and request of the U. S. Public Health Service. The exhibit is located in the U. S. Government Building; the space available did not permit such an extensive display as at Chicago, but it has been arranged by those named to bring pharmacy and its public health service to the attention of the visitors. Dr. R. C. Williams, Assistant Surgeon General, U. S. Public Health Service, is in charge of the Exhibit, portraying scientifically the "Story of Life," and the Pharmacy Exhibit is one of this group. The story begins with the geological investigation in Utah and other sections by the Smithsonian Institution and is carried through the evolution of animal life and finally to man, including his diseases and the methods he has developed for preventing and treating them. The exhibits of the public health professions are arranged to show their relation to each other and the laity. Pharmaceutical relics and equipment will also illustrate the development of pharmacy in Texas.

Bulletin No. 16 has been drawn upon for the basis of this comment. The AMERICAN PHARMACEUTICAL ASSOCIATION will convene August 24th–29th, in Dallas, and members will have the opportunity to visit the Texas Centennial Exposition. Each annual convention of the ASSOCIATION has its special attractions and affords attending members an opportunity to become acquainted with the section of the country in which the meeting is held and to study the problems of its druggists and pharmacists.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; Glenn L. Jenkins, John C. Krantz, Jr., Heber W. Youngken, L. W. Rowe, L. W. Rising, C. O. Lee, E. V. Lynn, W. G. Crockett, Frederick V. Lofgren.

THE POTENCY OF ELEVEN CRYSTALLINE CARDIAC PRINCIPLES FROM PLANTS.*,[1]

BY K. K. CHEN, A. LING CHEN AND ROBERT C. ANDERSON.

In connection with our work on bufagins and bufotoxins isolated from the paratoid secretions of different species of toads (1), comparative studies were made with several crystalline substances of plant origin reported to have a digitalis-like action. In view of the fact that they have never been assayed under the same conditions, the presentation of our data may prove helpful to other workers who are interested in their relative activity. Furthermore, the differences in potency noted in this work may throw some light upon the significance of certain groups in their chemical structure and stereoisomerism, since progress in this field has been rapidly made (2), (3). The list includes convallatoxin, β-antiarin, ouabain, cymarin, scillaren A, uzarin, digoxin, digitoxin, gitoxin, erythrophlein sulphate and thevetin. With the exception of erythrophlein, which is an alkaloid of *Erythrophlæum guineense*, the other compounds are glucosides. The authors are indebted to Dr. W. A. Jacobs, the Rockefeller Institute for Medical Research, New York City, for a generous supply of cymarin, to Professor R. L. Stehle, McGill University, Montreal, for that of scillaren A, and to Dr. R. Tschesche, University of Göttingen, Germany, for that of uzarin and β-antiarin. Thevetin was isolated by ourselves from *Thevetia neriifolia* (4), while ouabain, erythrophlein sulphate and digitoxin were purchased from Merck and Company, Rahway, New Jersey, convallatoxin from Hoffmann-La Roche, Inc., Nutley, New Jersey, and digoxin and gitoxin from Burroughs Wellcome and Company, Tuckahoe, New York. The last two principles were first isolated by Smith from *Digitalis lanata* (5).

Of the eleven compounds, gitoxin is so insoluble in alcohol or water that its action and potency could not be accurately determined. The remaining substances are soluble in dilute alcohol. Ouabain and erythrophlein sulphate are the only members that are completely soluble in water. In our experiments, a stock solution of each to contain 0.1 per cent of the drug was prepared. Cymarin, scillaren A, digoxin and digitoxin required 47.5 per cent ethyl alcohol to effect solution (one part 95 per cent alcohol and one part saline), and convallatoxin and β-antiarin 28.5 per cent (three parts 95 per cent alcohol and seven parts water). With thevetin, 19 per cent alcohol was employed. Both ouabain and erythrophlein were dissolved in saline. Uzarin was made up into 1 or 2 per cent solution in 47.5 per cent alcohol. Appropriate dilutions were then made from the stock solution for the tests desired.

It may be pointed out that erythrophlein is the only alkaloid known to have a digitalis-like action (6), (7). The specimen (in the form of a sulphate) we obtained

* From the Lilly Research Laboratories, Indianapolis, Indiana.

[1] Scientific Section, A. PH. A., Portland meeting, 1935.

Fig. 1.—Action of Erythrophlein on Frog's Heart. Frog No. 567, female, weighing 61 Gm., was decerebrated and pithed. At arrow, the heart was perfused with erythrophlein sulphate, 1:50,000, *via* inferior vena cava.

was beautifully crystalline, and when heated in a capillary tube immersed in an oil bath it began to soften at 68° C., became a clear viscous mass at 88° C., and decomposed with evolution of gas at 140° C. The substance reduced Tollen's reagent but gave negative results with Legal, Liebermann-Burchard and Sakaguchi tests. Combustion analyses yielded the following figures:

C 59.12; H 8.24; N 3.12; S 2.42
C 59.15; H 8.31; N 3.09; S 2.53

It is possible that Harnack's empirical formula (8), $C_{28}H_{43}NO_7$ or $C_{28}H_{45}NO_7$, needs revision.

By perfusion into the inferior vena cava in frogs according to the method of Howell and Cooke (9), A-V dissociation and ventricular systolic standstill were demonstrated, as shown in Fig. 1. Convincing evidence of the digitalis-like action of erythrophlein sulphate on the mammalian heart such as that of the cat was recorded on the electrocardiogram by following the technique previously described (10), a 1:50,000 solution being injected intravenously at the rate of 1 cc. per minute. Figure 2 may be taken as an example to illustrate P-R prolongation, bradycardia, ectopic rhythm, secondary tachycardia, and finally ventricular fibrillation. In addition, the alkaloid caused nausea and vomiting in both pigeons and cats so that there is no doubt about its digitalis-like effect.

Regarding uzarin Gessner (11) observed systolic standstill of the amphibian ventricle either by perfusion or *in situ*. In our studies it was found that in frogs (*Rana pipiens*) a 1:5000 solution perfused into the inferior vena cava caused a moderate slowing of the heart rate and some decrease in amplitude of contractions, but no systolic stoppage. By injection into the lymph sac in frogs, however, large doses induced systolic standstill.

1. The Hatcher-Brody Method (12).—The solutions of the substances were so adjusted that when injected into the femoral vein at the rate of 1 cc. per minute they would kill a cat weighing less than 3 Kg. within about $1^1/_2$ hours. This time limit was arbitrary but seemed to be

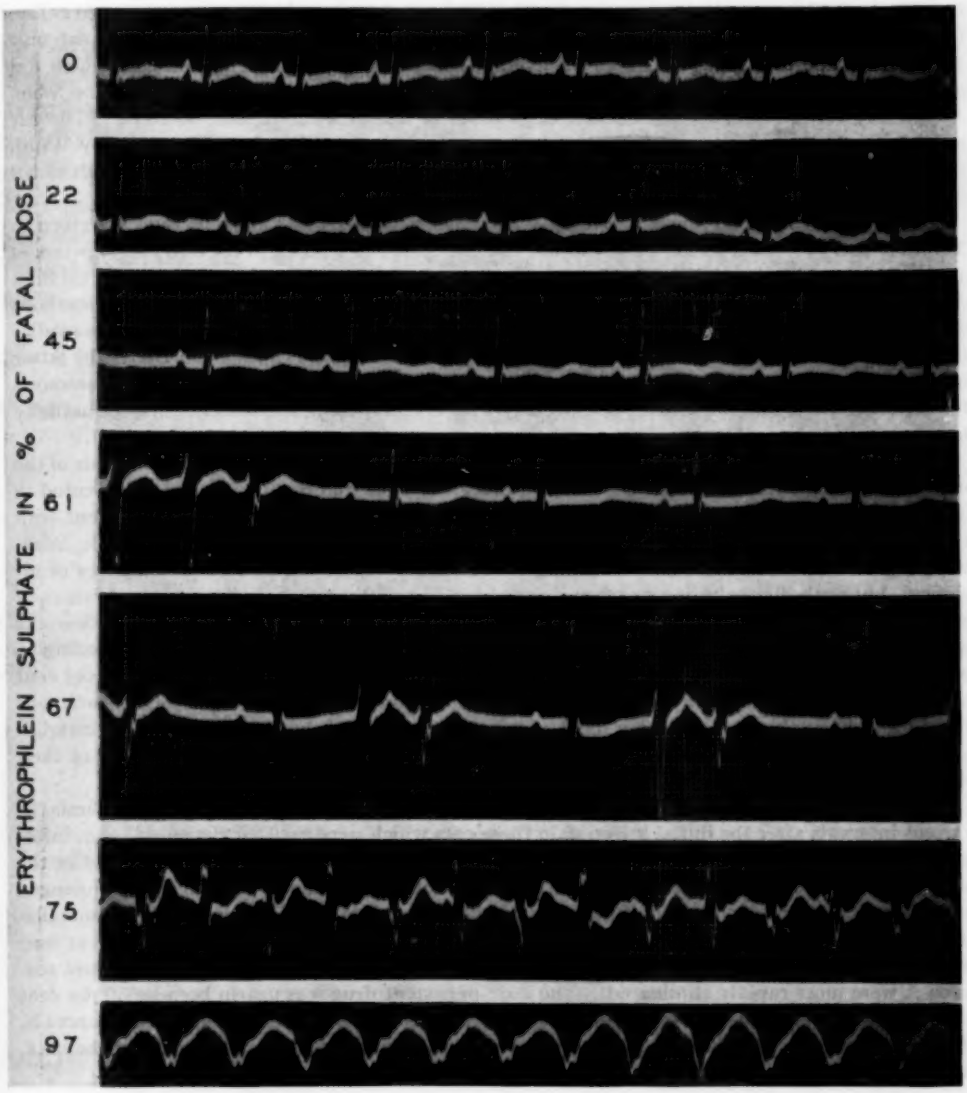


Fig. 2.—Electrocardiographic Changes Caused by Erythrophlein. Cat No. 1392, female, weighing 2.068 Kg., was anesthetized by ether. Erythrophlein sulphate in 1:50,000 solution was injected into the femoral vein at the rate of 1 cc. per minute. A total of 28 electrocardiograms was taken from lead II at different stages of this experiment. Only 7 selected tracings are shown in the figure. The abscissal time-lines make divisions equal to 0.02 and 0.10 second, and the ordinates those representing 0.0001 and 0.0005 volt.

suitable for both the easily eliminated compounds, such as ouabain, and the slowly acting ones, such as digitoxin. A stethoscope was used for the determination of the end-point. A group of 10 or more animals was employed in order to obtain an average of some statistical significance. The results are shown in Table I and summarized in Table IV. It should be noted that ouabain,

which for a long time has been known as the most potent of all cardiac glucosides, now ranks third according to the cat unit. The superiority of convallatoxin to ouabain in frogs has been noted by Karrer (13). Previously (1), it was shown that four bufagins were more powerful than ouabain. It may also be pointed out that in a series of 53 animals the cat unit of thevetin was found to be 0.92 mg. per Kg. as compared with 0.85 mg. in 16 cats, which has been reported before (14). The potency of uzarin is very low and variable. As indicated in Table I, the cat unit varied from 1.83 to 8.33 mg. per Kg., the average being 5.08 mg. There were 2 cats which did not die even with 14.5 and 13.2 mg. per Kg., respectively. They were not included in the table. Apparently certain animals can tolerate huge doses of uzarin without fatal outcome. The cat unit of digoxin in our series of experiments is equal to just one-half of that reported by White (15). Without knowing the strength of his solution and speed of his injection, it is difficult to account for the discrepancy.

2. The U. S. P. Frog Method (16).—The results by this well-known method are given in Tables II and IV. As a whole, they bear out the same order of activity of the different substances as that obtained by the cat method, except that thevetin in frogs proves to be more powerful than digitoxin and erythrophlein, while in cats the reverse is true. Quantitatively, the two methods do not yield the same ratio of activity among the different principles. For example, convallatoxin is fully 38 times as active as digitoxin in frogs, but is only 4.3 times as potent as the latter in cats. In some instances the difficulty of absorption in frog's lymph sac apparently accounts for the differences, but in a few cases, especially with erythrophlein, the material may be actually less poisonous to frogs than to cats.

3. The Cat Minimal Emetic Dose.—In previous reports (1), (17), mention was made of the minimal emetic doses of several substances. More complete and detailed data are presented in Table III. With convallatoxin, β-antiarin and ouabain, a 1:2000 solution was adopted, but with the remaining compounds a 1:1000 solution was employed. All injections were made intravenously in unanesthetized cats. Vomiting occurred in 10 to 15 minutes in the majority of instances, but with digitoxin, it was often delayed for 30 to 50 minutes, indicating its slowness of action. An examination of Table IV at once shows that the emetic effect does not follow the cardiac action, a phenomenon already observed by Eggleston and Hatcher (18). According to our data uzarin is the most powerful in causing vomiting. A dose equivalent to about 7 per cent of the average cat unit, rapidly injected, was sufficient to induce emesis in the majority of animals. Erythrophlein sulphate, on the other hand, required 81 per cent of the average cat unit as its minimal emetic dose. With the remaining substances, they varied from 24 to 75 per cent of their respective cat units.

4. Persistence of Action.—By determining the fatal dose under ether anesthesia at various intervals after the initial injection in those cats which were used for the emesis test, information may be obtained regarding how long each substance stays in the body or is fixed in the heart; in other words, the persistence of action. Digitoxin was found to have the most prolonged effect, for 38 per cent of the cat unit persisted for more than 5 days. Digoxin, cymarin, convallatoxin and erythrophlein sulphate proved to be relatively persistent since one-half of the cat unit in each case remained in the circulation for 1 to 7 days. β-Antiarin, ouabain, thevetin and scillaren A were more rapidly eliminated. The least persistent drug was uzarin because 50 per cent of the cat unit often disappeared within an hour. The order of persistence of these substances is, therefore, digitoxin, digoxin, cymarin, convallatoxin, erythrophlein, β-antiarin, ouabain, thevetin, scillaren A and uzarin.

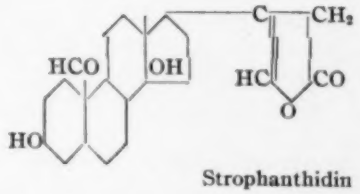
DISCUSSION.

Table IV clearly indicates that there is a disagreement of the results by three different methods of assay. It appears that digitoxin and erythrophlein are inherently more potent to feline than to amphibian hearts. The cat minimal emetic dose does not follow the frog's minimal systolic dose or cat unit. These data will be of importance from a therapeutic point of view, for none of the newer products should be applied to men unless their exact potency is known. The clinicians in this country appear to prefer the cat unit instead of the frog minimal systolic dose (19), (20).

The results are also interesting from a chemical point of view. It is now well known that upon hydrolysis the cardiac glucosides yield aglucones of C_{23} derivatives and one or more molecules of a sugar or sugars (21), (22), (23), (24). Scillaridin A, the aglucone of scillaren A, however, conforms to the C_{24} formula (25). Furthermore, many of the bufagins which occur in toad poisons and which are closely related to aglucones, do not have the C_{23} pattern (17). The structural formulas of several aglucones have been proposed and in certain instances established with certainty. They are derivatives of cyclopentenophenanthrene with an unsaturated lactone side chain. A consideration of our results in light of the following equations should be, therefore, of some interest. These structural formulas were suggested by Jacobs and Elderfield (26), Kon (27), Tschesche and Bohle (28), Tschesche and Haupt (29), Stoll, Hofmann and Helfenstein (25), Smith (30) and Elderfield (31).

$C_{30}H_{44}O_9 + H_2O \longrightarrow C_7H_{14}O_4$
Cymarin — Cymarose

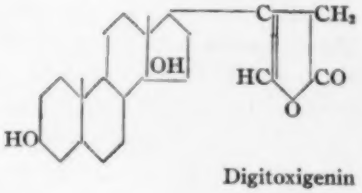
+



Strophanthidin

$C_{41}H_{64}O_{13} + 3H_2O \longrightarrow 3C_6H_{12}O_4$
Digitoxin — Digitoxose

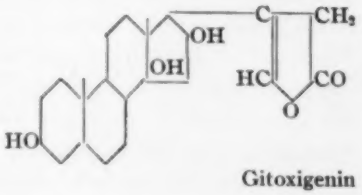
+



Digitoxigenin

$C_{41}H_{64}O_{14} + 3H_2O \longrightarrow 3C_6H_{12}O_4$
Gitoxin — Digitoxose

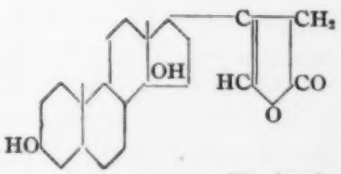
+



Gitoxigenin

$C_{35}H_{54}O_{14}.2H_2O \longrightarrow 2C_6H_{12}O_6 + H_2O$
Uzarin — Glucose

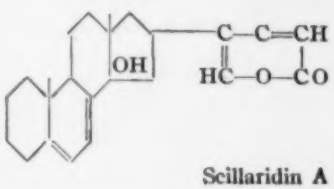
+



Uzarigenin

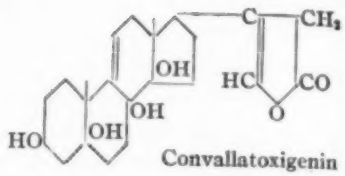
$C_{36}H_{52}O_{13} + H_2O \longrightarrow C_6H_{12}O_6 + C_6H_{12}O_5$
Scillaren A — Glucose — Rhamnose

+



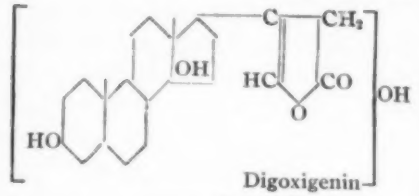
Scillaridin A

$C_{29}H_{42}O_{10} + H_2O \longrightarrow C_6H_{12}O_5$
Convallatoxin Rhamnose



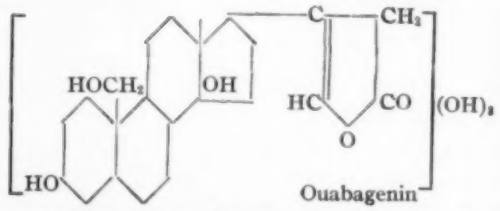
Convallatoxigenin

$C_{41}H_{64}O_{14} + 3H_2O \longrightarrow 3C_6H_{12}O_4$
Digoxin Digitoxose



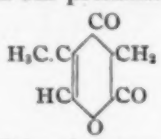
Digoxigenin

$C_{29}H_{44}O_{12} + H_2O \longrightarrow C_6H_{12}O_5$
Ouabain Rhamnose

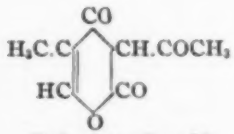


Ouabagenin

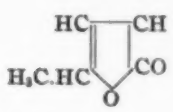
The most significant feature is that uzarin, which has an aglucone isomeric with digitoxigenin, has a very feeble cardiac action. The difference in steric arrangements probably accounts for the difference in their activity. Among the active members, the variation in potency is very great. For example, digoxin is 275 per cent, and digitoxin 412 per cent, less powerful than convallatoxin, gram for gram. It is possible that the two hydroxyl groups on C^5 and C^8 and the double bond between C^9 and C^{11} in the convallatoxigenin molecule are of significance in contributing to the high potency of convallatoxin. One is tempted to postulate that the presence of a carbinol group on C_{10} in the aglucone molecule of ouabain, and that of an aldehyde group on the same C-atom in the aglucone molecule of cymarin are also favorable to the high cardiac activity of the two substances. The sugar component alone has no action on the heart, but when conjugated with an aglucone it increases the potency (32). There is some suggestion from the results that the glucose-containing glucosides are rapidly eliminated while the digitoxose- or cymarose-containing members have a persistent action. The cyclopentenophenanthrene ring system apparently has no effect on the heart, for estrogenic hormones, bile acids and sterols have never been reported to stimulate the vagus or affect the myocardium like digitalis. The most important parts of the molecule are undoubtedly the double bond and the lactone ring, for hydrogenation and saponification both result in loss of activity (33), (34), (35), (36). It will be interesting to investigate pharmacologically the lactone side chains (α-pyrone and 2,3-dihydro-α-furone) of certain aglucones without the sterol ring system attached to them. The simple unsaturated lactones as listed below are devoid of any digitalis-like action, as concluded from our preliminary studies.



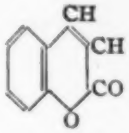
Triacetic lactone



Dehydracetic acid



α-Angelica lactone



Coumarin

The digitalis-like action of the alkaloid erythrophlein is of unusual interest. The negative Sakaguchi test indicates that the compound does not belong to the group of bufotoxins which also contains nitrogen. The failure of the sodium nitroprusside test makes it deviate from the constitution of common aglucones. As yet, there is no evidence that erythrophlein is a derivative of cyclopentenophenanthrene. The elucidation of its structure may thus lead to the discovery of another type of substances having a digitalis-like action but differing structurally from aglucones, bufagins and bufotoxins.

SUMMARY.

The potency of 11 crystalline digitalis-like substances—convallatoxin, β-antiarin, ouabain, cymarin, scillaren A, digoxin, digitoxin, erythrophlein sulphate, thevetin, uzarin and gitoxin—has been compared under the same conditions by the cat unit, the frog minimal systolic dose and the cat minimal emetic dose. Both convallatoxin and β-antiarin are more powerful than ouabain. The cat unit of thevetin should be revised to 0.92 ± 0.035 mg. per Kg. instead of 0.85 as previously reported.

The emetic action does not run parallelly with the cardiac action. Uzarin having the least cardiac effect is very highly efficient in causing vomiting.

The order of persistence of action from high to low is digitoxin, digoxin, cymarin, convallatoxin, erythrophlein, β-antiarin, ouabain, thevetin, scillaren A and uzarin.

Gitoxin is so insoluble in alcohol and water that its cardiac action cannot be accurately determined.

The significance of certain chemical structures with reference to their pharmacological activity has been discussed.

TABLE I.—CAT UNITS OF 10 CARDIAC PRINCIPLES OF PLANT ORIGIN.

Drug.	Solution.	Cat No.	Sex.	Weight, Kg.	Fatal Dose, Mg. per Kg.	Drug.	Solution.	Cat No.	Sex.	Weight, Kg.	Fatal Dose, Mg. per Kg.
Convallatoxin	1:400,000	1438	M	2.477	0.06	Digitoxin	1:100,000	491	M	1.459	0.37
		1439	F	1.848	0.06			492	M	1.944	0.32
		1440	F	1.889	0.08			494	F	1.590	0.34
		1441	F	2.537	0.08			495	M	1.452	0.41
		1442	M	2.798	0.08			496	M	1.608	0.28
		1445	F	2.489	0.06			501	F	1.647	0.34
		1449	F	2.261	0.09			502	F	1.800	0.34
		1450	F	2.406	0.10			503	M	1.512	0.27
		1451	F	1.707	0.07			504	F	1.972	0.31
		1452	F	1.823	0.08			505	M	1.733	0.31

TABLE I.—CAT UNITS OF 10 CARDIAC PRINCIPLES OF PLANT ORIGIN.—(*Continued from page 585.*)

Drug.	Solution.	Cat No.	Sex.	Weight, Kg.	Fatal Dose, Mg. per Kg.
β-Antiarin	1:200,000 and 1:100,000	1444	F	2.381	0.13
		1446	F	1.632	0.11
		1447	F	1.915	0.12
		1448	F	2.737	0.12
		1453	F	2.543	0.07
		1454	M	2.879	0.10
		1455	F	2.227	0.09
		1456	F	2.634	0.12
		1457	F	2.120	0.09
		1458	M	2.076	0.09
Ouabain	1,100:000	30	F	2.290	0.14
		31	F	1.830	0.15
		32	F	2.264	0.09
		33	M	1.846	0.10
		34	F	2.815	0.11
		35	F	2.417	0.14
		36	F	2.171	0.14
		37	F	2.703	0.10
		40	M	2.353	0.13
		41	M	2.660	0.11
		42	M	2.967	0.12
		43	M	1.846	0.14
		44	F	2.828	0.12
		45	F	1.750	0.12
		98	M	2.157	0.11
		99	M	2.263	0.12
		100	M	2.135	0.12
		101	M	2.155	0.13
		102	M	1.928	0.11
		129	M	2.114	0.11
		130	F	2.286	0.11
		131	F	2.215	0.11
		558	M	1.492	0.15
		559	F	1.411	0.13
		560	F	1.713	0.12
		561	M	2.409	0.11
		562	F	1.880	0.17
		563	M	2.011	0.12
		564	F	1.958	0.10
		565	M	1.826	0.13
		566	M	1.553	0.13
		567	M	1.790	0.10
		699	F	2.330	0.10
		698	M	2.273	0.09
		700	M	2.280	0.13
		701	F	2.261	0.12
		702	F	1.990	0.12
		1144	F	1.793	0.15
		1145	F	1.830	0.14
		1146	M	2.151	0.15
Erythrophlein Sulphate	1:50,000	506	F	1.891	0.29
		538	F	1.519	0.36
		1169	F	1.650	0.48
		1170	M	2.064	0.42
		1171	M	2.740	0.34
		1172	F	2.310	0.55
		1173	F	2.245	0.34
		1174	M	2.210	0.30
		1175	F	2.758	0.36
		1176	F	2.470	0.38
		1177	M	3.060	0.28
		1178	M	2.651	0.32
		1179	F	2.052	0.30
Thevetin	1:20,000	1070	M	2.124	0.85
		1071	M	1.800	0.69
		1072	M	1.880	0.67
		1073	F	1.785	0.70
		1074	F	2.274	0.83
		1079	F	2.186	0.79
		1080	F	1.775	0.79
		1081	M	1.992	0.81
		1082	F	1.762	1.36
		1083	M	1.808	0.77
		1084	F	2.140	1.36
		1085	F	2.060	0.67
		1086	F	2.850	1.24
		1089	M	1.536	0.62
		1090	M	3.300	0.59
		1091	M	1.720	0.80
		1291	M	2.436	0.93
		1290	F	2.314	1.04
		1229	F	2.370	0.63
		1228	F	2.855	0.60
		1259	F	1.690	1.14
		1257	F	2.184	0.84
		1256	F	2.292	0.61
		1260	M	1.951	0.80
		1258	F	1.533	0.72
		1253	F	2.209	0.63
		1254	M	2.480	0.65
		1255	F	2.111	1.14
		1244	F	2.422	1.75
		1242	F	2.837	0.68
		1240	F	2.495	1.00
		1241	M	1.910	0.78
		1238	M	2.070	0.94
		1236	F	1.924	0.77
		1237	F	2.470	1.20
		1269	F	2.157	1.16
		1264	F	2.607	1.72

Cymarin 1:100,000	1147	M	2.360	0.12	Uzarin 1:3000	1266	M	2.739	1.34
	1148	M	2.333	0.11		1265	F	2.457	1.17
	1149	F	1.646	0.12		1263	F	2.185	0.99
	1150	F	1.962	0.12		1262	M	2.697	1.03
	1151	F	1.964	0.11		1261	F	2.423	1.47
	1152	F	1.990	0.11		1271	F	2.177	0.88
	1153	F	2.034	0.12		1270	F	2.260	1.19
	1154	F	1.822	0.13		1280	F	2.006	0.98
						1278	F	2.128	1.06
Scillaren A 1:100,000	594	F	1.762	0.19		1224	F	3.215	0.83
	595	F	2.608	0.09		1223	M	3.025	0.56
	596	M	1.770	0.16		1166	F	2.290	0.88
	597	F	1.765	0.16		1165	M	1.818	0.99
	598	M	1.827	0.21		1168	F	2.283	0.81
	602	F	2.073	0.15		1167	M	2.116	0.91
	603	M	1.612	0.15		1109	F	2.196	0.83
	604	F	1.749	0.14		1110	F	1.955	0.87
	605	F	2.155	0.11		1111	F	2.260	0.76
	606	F	1.700	0.15		1106	M	2.145	0.82
						1107	F	2.773	1.15
						1108	F	2.833	0.74
Digoxin 1:100,000	1198	M	2.265	0.28					
	1199	F	1.955	0.28		1402	F	1.889	3.07
	1200	M	2.290	0.17		1403	F	1.960	6.72
	1201	M	2.528	0.26		1404	F	1.764	2.91
	1202	M	1.882	0.25		1405	M	1.600	1.83
	1203	F	2.075	0.23		1406	F	1.565	5.98
	1204	F	1.910	0.21		1407	F	2.543	3.85
	1205	F	1.830	0.24		1410	F	2.537	7.96
	1206	M	2.538	0.17		1418	F	2.100	3.62
	1207	M	1.830	0.22		1420	F	2.023	6.52
						1421	F	2.717	8.33

TABLE II.—FROG MINIMAL SYSTOLIC DOSES OF 10 CARDIAC PRINCIPLES OF PLANT ORIGIN.

Drug.	Solution.	Dose, Mg. per Kg.	No. in Systolic Standstill/ No. of Frogs Used.
Convallatoxin	1:40,000	0.00014	0/4
		0.00018	2/8
		0.00021	3/4
		0.00025	3/4
β-Antiarin	1:20,000	0.00032	1/4
		0.00035	1/4
		0.00039	10/16
		0.00043	4/4
Ouabain	1:20,000	0.00040	0/4
		0.00045	0/4
		0.00050	3/4
		0.00055	4/4
Cymarin	1:20,000	0.00050	0/4
		0.00055	0/4
		0.00060	3/4
		0.00065	3/4
		0.00070	4/4
Scillaren A	1:20,000	0.00065	0/7
		0.00070	7/12
		0.00075	4/7

TABLE II.—(*Continued from page 587.*)

Drug.	Solution.	Dose, Mg. per Kg.	No. in Systolic Standstill/ No. of Frogs Used.
Digoxin	1:5000	0.00225	1/4
		0.00250	3/4
		0.00300	7/8
Digitoxin	1:2000	0.00650	0/4
		0.00700	3/12
		0.00750	4/8
		0.00800	6/8
		0.00850	4/4
Erythrophlein Sulphate	1:1000	0.01000	1/4
		0.01100	5/8
		0.01200	3/4
		0.01300	7/8
Thevetin	1:2000	0.00400	0/12
		0.00450	18/24
		0.00500	7/8
Uzarin	1:50	1.00000	1/4
		1.10000	0/1
		1.20000	0/1
		1.30000	0/1
		1.40000	0/3
		1.50000	2/3

TABLE III.—MINIMAL EMETIC DOSES OF 10 CARDIAC PRINCIPLES OF PLANT ORIGIN IN CATS.

Drug.	Dose, Mg. per Kg.	No. of Cats Vomited/ No. of Cats Used.
Convallatoxin	0.050	0/2
	0.060	2/3
	0.070	2/3
	0.080	2/2
β-Antiarin	0.030	0/3
	0.040	2/2
	0.050	2/2
Ouabain	0.050	0/2
	0.060	2/3
	0.070	2/2
Cymarin	0.070	0/3
	0.080	3/3
	0.090	2/2
Scillaren A	0.080	1/3
	0.090	1/3
	0.100	2/2
Digoxin	0.060	0/2
	0.070	2/2
	0.080	2/3
Digitoxin	0.100	0/2
	0.125	1/3
	0.150	2/2
Erythrophlein Sulphate	0.200	0/2
	0.250	1/3
	0.275	1/3
	0.300	2/2

	0.200	0/2
	0.225	2/3
Thevetin	0.250	2/2
	0.275	2/2
	0.300	2/2
	0.300	0/2
	0.325	0/2
Uzarin	*0.350*	2/3
	0.400	1/1
	0.500	1/1

TABLE IV.—SUMMARY OF ALL RESULTS.

Drug.	Cat Unit (Mean ± Probable Error), Mg. per Kg.	Frog Minimal Systolic Dose, Mg. per Kg.	Minimal Emetic Dose in Cats, Mg. per Kg.
Convallatoxin	0.08 ± 0.002	0.00021	0.060
β-Antiarin	0.10 ± 0.004	0.00039	0.040
Ouabain	0.12 ± 0.002	0.00050	0.060
Cymarin	0.13 ± 0.003	0.00060	0.080
Scillaren A	0.15 ± 0.007	0.00070	0.100
Digoxin	0.22 ± 0.008	0.00250	0.075
Digitoxin	0.33 ± 0.008	0.00800	0.150
Erythrophlein Sulphate	0.37 ± 0.017	0.01100	0.300
Thevetin	0.92 ± 0.035	0.00450	0.225
Uzarin	5.08 ± 0.437	1.50000	0.350
Gitoxin*	Unable to determine	Unable to determine	Unable to determine

* Insoluble.

The authors are indebted to Dr. A. M. Van Arendonk and Messrs. Chester C. Hargreaves and Brown Robbins for their valuable assistance in this work.

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STRYCHNINE VI. VARIATION IN PHYSIOLOGICAL ACTION OF C.P. STRYCHNINE.*

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For many years, men using strychnine alkaloid for the control of noxious rodents and predatory animals have noticed variation in the results obtained. The earlier explanations were that variations in field and animal conditions or in the methods of placing the poison baits were responsible. It was incredible that a substance as chemically stable as strychnine would not be uniform in its toxic properties. Wide-spread complaints, traceable to the same lot of poison, have become so prevalent within the past few years, however, that we have been forced to recognize the probability that something was wrong with those lots.

Since we had, for several years, been running tests for the "free base," and the crystal size of the incoming lots of alkaloid, we made an attempt to associate the per cent of free base or the physical size of the particles with the reported troubles. There was no correlation—in fact, the alkaloid carrying the lowest free base very often proved the most efficient toxic agent, and the crystal size was entirely too variable a factor for any conclusions to be drawn. The most toxic alkaloids and the least toxic were often practically the same size—either large or small.

During the past few years, the Denver laboratory has tested biologically 27 lots of the alkaloid, originating from five wholesale distributors. Our system of tests has been by means of stomach tube to white rats. A test suspension of the alkaloid in the concentration of 1 mg. of strychnine to each cc. of suspension was made with the assistance of 1 per cent acacia. The animals to be used were weighed and divided into comparable series. The doses were computed for each animal, and the dose for the first rat measured out in a hypodermic syringe. The animal was then placed on a holding board and a wooden gag, having a $^3/_{16}$" hole in it, was placed in its mouth. A No. 8 soft rubber catheter was then passed through the hole in the gag into the animal's stomach. The syringe was shaken to insure

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* Scientific Section, A. PH. A., Portland meeting, 1935.

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uniform suspension, and the dose administered. A 1-cc. rinse was forced through the catheter, which was then removed, and the animal placed back in the cage for observation. The time at which the dose is administered, and that of the first spasm are recorded, as well as the time until the stoppage of the heart.

We use 25.00, 22.50, 20.00, 17.50, 15.00, 12.50, 10.00, 7.50 and often 6.00 mg. per Kg. body weight as our standard series of doses for preliminary trials. Two rats are desired for each dose in preliminary work, and ten for each in confirmatory tests. Certain digressions from this plan were necessary during the work herein reported, owing to lack of sufficient uniform animals.

Table I shows the differences in the physical and chemical examinations, as well as the variations in killing ability of these poisons. From this table it appears that fifteen of the twenty-seven alkaloids were tested on eleven or more animals. The other twelve samples were tested on five animals to the series, and are consequently useful largely for corroborative data. It also appears that Samples A-1 and B-1 show the greatest difference in toxicity. A careful study of these extremes was made to confirm our observations of a more general nature. Table II gives our tests with these two alkaloids in detail.

TABLE I.—CHEMICAL AND BIO-ASSAY OF STRYCHNINE ALKALOIDS.

Manufacturer.	Sample Number.	Alkaloidal Content, %.	$LD_{100\%}$ Rats, Mg./Kg.
A	1	99.31	Over 25
	2	...	Over 25
	3	...	20
	4	...	20
	5	...	17.5
	6	...	17.5
	7	...	15
	8	...	15
	9	99.70	12.5
	10	...	Below 10
B	1	98.86	7.5
	2	98.91	7.5
C	1	...	20
	2	98.68	15
	3	...	12.5
	4	...	7.5
	5	...	7.5
	6	...	7.5
D	1	...	20
	2	98.28	15
	3	99.30	15
	4	...	15
	5	...	12.5
	6	...	10
E	1	...	12.5
	2	...	10
	3	98.60	7.5

To demonstrate that this wide variation is not altogether due to possible faulty technique or to an unexpectedly wide difference in physiological responses,

TABLE II.—COMPARATIVE TOXICITY OF STRYCHNINE ALKALOIDS A-1 AND B-1; STOMACH TUBE ADMINISTRATION TO WHITE RATS.

Sample.	25.0. T/S.[1]	T/D.[2]	20.0. T/S.	T/D.	15.0. T/S.	T/D.	12.5. T/S.	T/D.	10.0. T/S.	T/D.	7.5. T/S.	T/D.
A-1— I	11.0	18.0	S[3]	S	S	S	S	S	S	S	..	..
II	4.5	6.5	..	..	6.0	9.5	..	..	..	..	7.0	10.0
	5.0	8.0			6.5	10.5					8.5	9.5
	7.5	9.0			7.0	9.0					14.0	19.0
	8.0	12.0			7.0	10.0					18.0	28.5
	8.0	16.0			12.5	20.0					26.0	31.0
	8.0	19.0			13.0	31.0					S	S
	9.0	10.5			15.0	21.0					S	S
	13.5	33.0			16.0	23.5					S	S
	16.0	32.0			24.0	32.0					S	S
	S	S			39.5	42.5					S	S
	S	S			..	..						
	S	S			..	..						
Av. II	8.8	16.2			14.7	20.9					14.7	19.6
B-1— I	8.0	13.0	9.0	15.0	12.0	15.0	9.0	13.0	10.0	15.0	..	..
II	5.0	8.5	..	..	4.0	5.0	..	..	..	..	6.5	8.5
	6.0	7.0			4.0	5.5					7.0	15.5
	6.0	7.5			5.0	14.0					9.0	13.0
	6.0	12.0			6.5	8.5					9.5	12.0
	6.0	12.0			8.0	11.0					11.5	18.0
	6.5	8.5			9.5	14.0					12.0	23.0
	7.5	12.0			12.0	17.0					12.5	15.5
	8.0	12.0			15.0	17.0					16.0	32.0
	14.0	16.0			16.0	18.5					26.0	27.5
	15.0	16.5			20.0	21.0					S	S
Av. II	8.0	11.20			10.0	13.2					12.2	18.3

FOOTNOTE: [1] T/S denotes time in minutes between administration and spasm.
[2] T/D denotes time in minutes between administration and death.
[3] S denotes survived.

TABLE III.—COMPARATIVE TOXICITIES OF A-1 AND B-1 AS THE SULPHATES; INTRAPERITONEAL INJECTIONS TO WHITE RATS.

Sample.	Dose: Mg./Kg. 10.00. T/S.	T/D.	7.5. T/S.	T/D.	5.0. T/S.	T/D.	4.0. T/S.	4.0. T/D.	3.5. T/S.	T/D.	3.25. T/S.	T/D.	T/S.	3.0. T/D.	2.75. T/S.	T/D.
A-1	2.0	5.0	1.0	7.0	3.0–4.0	9.0–8.0	4.0–4.0	5.0–6.0	7.0	21.0	4.0	7.0	8.0–14.0	20.0–16.0	10.0	13.0
B-1	3.0	5.0	3.0	4.0	3.0–2.0	15.0–3.0	5.0–2.0	12.0–4.0	3.0	5.0	9.0	15.0	10.0	12.0	S	S

Av. A-1: T/S— 5.5
T/D—10.6.

Av. B-1: T/S—4.4
T/S—9.0.

we prepared the sulphates from the two alkaloids and administered the solutions of these salts by intraperitoneal injection. Table III gives the results of this test. This tabulation shows that although the differences are smaller, they are still in the same direction.

A further test was made using laboratory-recrystallized alkaloids in comparison with the original commercial products. Six different lots of the commercial material were recrystallized in the laboratory and the twelve lots of poison thus obtained were tested. The laboratory-recrystallized product had a fairly uniform crystal size, whereas the original alkaloids were decidedly variable. The commercial alkaloid and the laboratory crystals from that alkaloid did not show any difference in toxicity.

CONCLUSIONS.

1. Commercial strychnine alkaloids of C.P. quality show definite and marked differences in toxicity.
2. These differences are of such magnitude that serious variation in results are noted in their use in economic poisons.
3. These differences have not been associated with determinable changes in chemical or physical properties.
4. Recrystallization of the various alkaloids does not alter their lethal efficiency.

THE INFLUENCE OF CERTAIN SALTS ON MORPHINE TOXICITY AND NARCOSIS IN MICE AND RATS.*

BY J. M. ORT AND W. G. CHRISTIANSEN.[1]

The study of synergism and antagonism among drugs has, admittedly, many fascinating theoretical and practical possibilities. In the field of morphine pharmacology, for instance, it is conceivable that certain drugs exist which can greatly potentiate the action of morphine in all of its manifestations, thus decreasing the dosage required. But, much more important, such a potentiator may some time be found which will affect only the narcotic action of the drug or at least will not proportionally increase its vicious habit-forming effects.

The influence of atropine on the activity of morphine is, of course, well recognized. F. Schmitz, for example, studied not only atropine in this connection but also lobelia, coramine, cardiazole, hexetone and pyramidon. (On the influence of central nervous stimulants on morphine poisoning (1).) W. Peters has reported that antipyrine is a morphine synergist. (A morphine-sparing ampul preparation (2).)

Bancroft (3) and his co-workers have made a most extensive study in this field, making use of the facts and theories of the modern science of colloid chemistry to expand the theory of anesthesia and the behavior of nervous tissues originally proposed by Claude Bernard. The essence of this theory is that anesthesia or narcosis results when the colloids of the cells of the nervous tissues are either abnormally reversibly dispersed or coagulated.

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* Scientific Section, A. PH. A., Portland meeting, 1935.

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Av. B-1: T/S—4.4 T/S—9.0.
Av. A-1: T/S— 5.5 T/D—10.6.

According to Bancroft's views morphine produces its effects by reversibly coagulating the cell colloids of the nervous system. These cells in the morphine addict, then, are over-coagulated. Morphinism, therefore, should yield to drugs which tend to disperse the cell colloids. The long recognized sedative action of bromides must be due to the ability of bromides to peptize the colloids of nerve tissue cells, to which property is also due whatever success has been realized in the treatment of morphinism with bromides. This theory demands that a drug which is a coagulating agent will serve to aggravate the effects of morphine and to prolong its action. Thus he found that sodium tartrate would appreciably prolong the effect of morphine in rabbits while sodium thiocyanate had the opposite effect in both rabbits and dogs.

The actual therapeutic value of sodium thiocyanate as an aid in restoring morphine addicts to health and happiness, the subject of considerable discussion and difference of opinion, need not be discussed in this paper. The importance of the fundamental principles involved, however, seemed to us to be so great as to justify still further pharmacological study. As the peptizer or disperser to test, we chose sodium thiocyanate, on which so much work has already been done by Bancroft. We selected mono-sodium phosphate as an example of a coagulator and sodium chloride as a somewhat intermediate compound. Morphine hydrochloride and acid phosphate were tested separately for comparison. Mice and rats were chosen as the test animals in order to make feasible a larger number of experiments, thus minimizing as far as possible the significance of individual biological variations.

There is, of course, a species difference in the response of various animals to morphine. Nevertheless, morphine is certainly a narcotic drug for mice and rats, and the fundamentals of its action in these animals must be considered as essentially parallel to those in man and the higher animals. Two things were investigated: toxicity and narcotic effect. The toxicities of the various combinations tested were determined in mice in terms of the M. L. D. of the morphine content of the combinations, that is, the single dose in mg./Kg. which will kill half of the animals receiving subcutaneous injections.

The narcotic activities of the various combinations tested were determined in several ways. L. Maier ("Quantitative Determination of Morphine by Bioassay" (4)) has further developed the method of Straub and Herrman in which the presence of morphine is manifested by the animal drawing up its tail over its back in an S-shape. The time between the injection and the onset of the reaction is recorded, as is also the duration of the reaction. O. W. Barlow in "The Tranquillizing Potency of Morphine, Pantopen, Codeine, Papaverine and Narcotine" (5) confined rats on their backs on boards and recorded their movements after their first excitement had worn off. Threshold or higher doses of the drugs decrease the number of these movements in a given period of time. We have found a tail pressure method to give perhaps the most accurate and consistent results of the three methods we tried. In this method a graduated cylinder containing mercury is carefully set on the rat's tail. By consecutive tests, the minimum height of mercury that will elicit a response from the animal is determined. As the morphine dosage is increased over the threshold dose, this height of mercury increases somewhat proportionally up to the point of complete anesthesia.

EXPERIMENTAL RESULTS.

All combinations tested were injected subcutaneously and prepared by adding the various ingredients to a 3% aqueous morphine hydrochloride solution in the proportion of 3 Gm. ingredient to 1 Gm. morphine hydrochloride, except that the morphine acid phosphate solution was prepared by adding 4 cc. of normal phosphoric acid to 0.2 Gm. of morphine alkaloid and then diluting to give a 3% solution.

TABLE I.—EFFECTS IN MICE.

	Mouse Toxicity.			"S" Tail Reaction.		
					Averages for Animals in Which Reactions Occurred.	
Material Injected.	No. of Animals Injected.	Approximate M. L. D. Mg./Kg.	Dose Mg./Kg. Morphine Hydrochloride Equivalent.	Incidence of Reactions.	No. of Minutes before Start of Reactions.	Duration of Reaction in Minutes.
Morphine Hydrochloride	65	300	5	3/15	37	120
			10	8/8	21	141
Morphine hydrochloride + mono-sodium phosphate	56	300	5	4/15	40	60
			10	8/8	28	116
Morphine hydrochloride + sodium sulphocyanate	49	90	5	10/16	40	65
			10	8/8	22	151
Morphine hydrochloride + sodium chloride	57	300	5	7/14	40	100
			10	8/8	38	101
Morphine acid phosphate	57	300	6	0/8	..	..

TABLE II.—NARCOTIC ACTIVITIES IN RATS.

	Tranquilizing Effect.		Response to Tail Pressure.			
			Relative Average Number of Movements of the Group after Injection as Compared to the Group Average of 100 before Injection.		Relative Pressure on Tail Required to Elicit Response after Injection as Compared to Pressure Necessary before Which Equals 100.	
Material Injected.	No. of Rats Tested.	Morphine Hydrochloride Equivalent Mg./Kg.	End 1st hr.	End 2nd hr.	End 1st hr.	End 2nd hr.
Morphine hydrochloride	5	1.67	60.3	39.1	100.2	122.2
	10	2.50	60.3	52.8	159.0	97.0
	10	3.75	45.2	60.3	236.8	211.0
	10	5.00	29.4	43.0	260.9	210.9
	10	7.50	28.9	29.5	513.1	351.8
Morphine hydrochloride + mono-sodium phosphate	5	1.67	50.0	33.3	133.0	143.0
	5	3.75	44.7	25.0	188.4	157.6
	5	7.50	4.8	34.9	578.4	299.4
Morphine hydrochloride + sodium sulphocyanate	5	1.11	28.6	14.3	110.4	118.0
	5	1.67	43.2	10.2	207.0	177.4
	5	3.75	60.2	53.4	238.8	248.4
	5	7.50	1.1	12.9	828.0	593.2
Morphine hydrochloride + sodium chloride	5	1.67	127.4	9.1	108.4	115.4
	5	3.75	69.8	37.2	241.4	206.0
	5	7.50	30.7	58.0	285.0	190.8
Morphine acid phosphate	5	1.67	51.5	12.1	149.4	111.5
	5	3.75	48.7	30.8	208.2	166.8
	5	7.50	0.0	0.0	326.0	299.8
Controls	26	..	51.7	28.1	117.8	127.4

DISCUSSION.

Toxicity—Table I.—It was found that for all the combinations tested, except that containing sodium sulphocyanate, the curve of dosage administered–incidence of death flattened out noticeably above a dosage of 150 mg./Kg. This makes an exact determination of M. L. D. for such combinations not only difficult but, for practical purposes, somewhat meaningless. No significant difference in M. L. D. could be determined among these four combinations. No consistent correlation could be detected between the incidence of death at a given dosage and the recent dietary history of the animals, *i. e.*, whether or not the animals had been fasted for 16 to 24 hours immediately preceding the test.

The results with the mixture of sodium sulphocyanate and morphine were much more sharp and consistent. The M. L. D. for this combination was definitely between 75 and 115 mg./Kg. and approximately at 90 mg./Kg. Thus our tests have shown that sodium sulphocyanate markedly increases the toxicity of morphine in mice when the two are injected simultaneously.

"S" Tail Reaction in Mice—Table I.—We found no outstanding difference in the behavior of the combinations, except that the morphine acid phosphate combination gave no response in the dosage tried. Certainly there is no evidence that mono-sodium phosphate potentiates morphine in mice or that sodium sulphocyanate antagonizes it. The results obtained by this method are apt to be irregular and inconsistent when intermediate doses are tested.

Tranquility Effect in Rats—Table II.—While this method also gave somewhat inconsistent results, it can again be seen that sodium sulphocyanate certainly does not appear to antagonize the action of morphine. The action of phosphates is seen to be irregular. With small dosages of morphine, there was little evidence of potentiation. In the largest dose tested, the tranquilizing effect of the morphine was increased by the phosphate at the end of the first hour—but so was it with sodium sulphocyanate.

Pressure on Rats' Tails Required to Elicit Responses—Table II.—This method gave us the most consistent results of the three methods tried. Comparing the effects, concentration by concentration, it is seen that, on the whole, both marked potentiation and marked antagonism of the morphine action are lacking. However, the most pronounced evidence of potentiation in this series of tests occurred with the combination of morphine and sodium sulphocyanate and the greatest evidence of antagonism was seen in the tests on morphine and sodium chloride mixtures.

SUMMARY AND CONCLUSIONS.

We are aware, of course, that, with respect to the relation between added ingredient and morphine, and to the dosage of morphine given, we have by no means studied exhaustively the possibilities of synergism and antagonism between morphine and sodium phosphate, chloride or thiocyanate. Our experiments were also confined to mice and rats. However, under the conditions of these experiments, we found on the whole no evidence of any marked increase or decrease of the action of morphine itself, either in the case of an added peptizer—sodium sulphocyanate—or added coagulators—mono-sodium phosphate and sodium chloride.

If anything, sodium sulphocyanate showed some tendency to potentiate the effect of morphine. It undoubtedly considerably increased its toxicity, which might be expected of any substance which could potentiate morphine in all of its manifestations. Our results are not those which could be predicted from Bancroft's theory on the mechanism of the pharmacological actions of morphine, sodium sulphocyanate and mono-sodium phosphate.

We gratefully acknowledge the assistance of the Biological Research Laboratories of E. R. Squibb and Sons in which all the tests on rats and mice reported herein were carried out.

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THE TOXICITY OF BARBITAL DERIVATIVES.*,[1]

BY IVOR JONES[2] AND E. V. LYNN.

Notwithstanding the large number of derivatives of barbituric acid which have been introduced into medicine, we have as yet only meager information as to comparative toxicity and efficiency. The textbooks make certain standard statements about the older ones which are not based upon existing evidence. Whatever reports can be found in the literature have originated largely in the laboratories of manufacturers, and the few unbiased records give very little data upon which the physician can base accurate judgment. The present study was designed as a start towards making such information available.

Of the marketed compounds seven of those most often used were selected for study: Barbital U. S. P. and phenobarbital U. S. P., introduced about 1904; dial, 1912; amytal, 1924; neonal, 1926; phanodorn, 1928; pentobarbital (nembutal), 1930.

The rabbit was chosen as the experimental animal because there seems no stated objection and several disadvantages have been found for other animals.

Using oral administration for rabbits, the M. L. D. in mg. per Kg. has been determined by Fitch and Tatum (1) as follows: Barbital 275, amytal 575, pentobarbital 175, phenobarbital 150, neonal 160, phanodorn 450. Roemer (2) gave for barbital 400. By subcutaneous injection in rabbits, the only results reported have been from the laboratories of Eli Lilly & Co.: Barbital 290, amytal 110, neonal 100. Intraperitoneally, Fitch and Tatum (1) gave: Barbital 225, amytal 90, pentobarbital 65, phenobarbital 150, neonal 115, phanodorn 130. Intravenously, Herwick and Knoefel (3) reported for barbital 250, for amytal 50. Intramuscularly, Louvier (4) gave for phenobarbital 150. As far as could be determined no one else has given any results on rabbits.

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* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] Seattle, Washington, June 19, 1934.

[2] Fellow of the National Conference on Pharmaceutical Research.

ORAL ADMINISTRATION.

In the present investigation, there were used only healthy animals of mixed breeds and of both sexes weighing four pounds or over, the females being in all cases non-pregnant. No variation in results because of sex was noticed in the preliminary experiments.

ORAL ADMINISTRATION.

Drug.	Dose, Mg. per Kg.	Number of Animals.	Result.
	300	4	S
Barbital	350	4	1
	375	4	1
	400	4	D
	100	4	S
Phenobarbital	125	4	1
	140	4	2
	160	4	D
	450	8	S
	500	4	1
	525	4	1
	550	2	S
	600	2	S
Amytal	650	2	S
	700	2	S
	800	2	S
	900	2	S
	1000	1	S
	1500	2	S
	100	4	S
Dial	125	4	2
	140	4	3
	100	4	S
Neonal	130	4	2
	150	4	3
	160	4	D
	200	2	S
	250	2	S
	275	2	S
	300	2	S
Pentobarbital	350	2	S
	400	2	S
	500	2	S
	600	2	S
	350	4	S
	400	4	S
Phanodorn	425	4	2
	450	4	2
	475	4	3

INTRAPERITONEAL INJECTION.

Drug.	Dose, Mg. per Kg.	Number of Animals.	Result.
	250	2	S
	275	2	S
	300	2	S
Barbital	325	2	S
	350	2	S
	375	2	1
	385	2	D
	140	2	S
Phenobarbital	150	2	1
	160	2	D
	170	2	D
	90	2	S
	100	2	S
Amytal	110	2	D
	125	2	D
	150	2	D
	90	2	S
Dial	100	2	1
	110	2	D
	125	2	D
	80	2	S
	90	2	S
Neonal	100	2	1
	110	2	1
	120	2	D
	40	2	S
	50	2	S
Pentobarbital	60	2	1
	70	2	1
	80	2	D
	90	2	D
	120	2	S
	140	2	S
	150	2	S
Phanodorn	160	2	1
	170	2	1
	180	2	D
	190	2	D

S = All survived. Figures are used for the number that died; the letter D signifies that all died; 1, one died; 2, two died; 3, three died.

During the period of experimental work the rabbits were fed twice daily with a constant diet of alfalfa hay and rolled barley. The animals were fasted for a period of sixteen hours before administering the drug. All of the rabbits were well housed and bedded on dry straw.

The dose of the drug was calculated upon body-weight to within one mg. and placed in several small gelatin capsules. These capsules were given by moistening them with water, placing them far down in the rabbit's throat, and then washing them down with a small volume of water. The time was noted as soon as an oral dose had been given and the period before partial and complete anesthesia was measured. The period of anesthesia and the various symptoms were observed and recorded. The minimum lethal dose was judged when 50 per cent of the animals died within thirty hours or during unconsciousness.

In the foregoing table are recorded the results of administration of the compounds orally to rabbits in varying doses.

INTRAPERITONEAL INJECTION.

The minimum lethal doses were determined by injecting carefully a freshly prepared solution of the drug into the peritoneal cavity of healthy rabbits. The solutions of the various compounds used were accurately prepared by dissolving a weighed sample of the product, furnished by the manufacturer, in a calculated amount of half-normal sodium hydroxide solution except, in the case of barbital, pentobarbital and phenobarbital, where the sodium salt of the hypnotic was available. Amytal, dial, neonal and phanodorn were dissolved in half-normal sodium hydroxide, the amount of solution needed for 1 Gm. of drug being 8.84 cc. for amytal, 9.60 cc. for dial, 9.42 cc. for neonal and 8.46 cc. for phanodorn. The solutions were then made up to the required volume in a calibrated glass cylinder by adding sterilized distilled water. In every case the final solution contained 100 mg. per cc. of the hypnotic as the free acid. In the case of barbital, pentobarbital and phenobarbital, the compound as the sodium salt was weighed out and dissolved in sterilized distilled water in such concentration that the final solution contained 100 mg. per cc. of the hypnotic as the free acid. With amytal, dial and neonal, complete solution was never obtained in the alkali used. Since the residue in any instance did not amount to more than a milligram or two out of two Gm., it was ignored as negligible.

The minimum lethal dose again was taken as that amount which caused death in 50 per cent of the animals within thirty hours or during anesthesia.

COMMENT.

The approximate minimum lethal doses are herewith summarized, together with those by Fitch and Tatum.

	Oral Administration.		Intraperitoneal Injection.	
	Present Report.	Fitch and Tatum.	Present Report.	Fitch and Tatum.
Barbital	385	275	375	225
Phenobarbital	140	150	150	150
Amytal	Above 1500	575	105	90
Dial	125	..	100	..
Neonal	135	160	110	115
Pentobarbital	Above 600	80	175	65
Phanodorn	450	450	170	130

The most striking differences from the former results are noted with oral doses of amytal and pentobarbital which we found practically non-lethal up to the figures given. In addition the period before appearance of complete anesthesia was always more or less uncertain. These facts would be best explained by incomplete or very slow absorption and application in human cases might be very different.

Another interesting observation is that the drugs are divided distinctly into two groups according to the degree of toxicity by oral administration. Those with a low dose (below 150) are dial, neonal and phenobarbital; the others are above 375. The ratio is, thus, 375:150 or about 2.5:1.

Comparison of the times required to produce anesthesia also furnished some interesting observations. In the table below the values given are in minutes following administration and the exact attainment of anesthesia was determined by loss of the corneal reflex.

	Orally.		Intraperitoneally.	
	Limits.	Usually.	Limits.	Usually.
Barbital	60–180	90	45–180	60
Phenobarbital	90–180	120	30–180	90
Amytal	60–240	120	10–15	10
Dial	60–240	90	20–60	45
Neonal	90–300	120	10–30	20
Pentobarbital	120–240	120	10–15	10
Phanodorn	60–240	90	10–60	30

From a study of these values, one could safely conclude that amytal and pentobarbital act at about the same rate and in the same manner. Both are the most rapidly acting of the entire group when given intraperitoneally. Barbital and phenobarbital are characterized by having essentially the same speed of action either orally or by injection. Except for barbital and phenobarbital, they all act very rapidly when injected, causing almost immediate paralysis of the limbs and flacidity of the abdominal muscles. The anesthetic action progresses until the animal is prostrated, with the eventual loss of the corneal reflex which has been taken as an indication of anesthesia. It should be noted here that, even with very large doses by mouth, amytal often paralyzed the animals for as long as thirty-six hours without giving loss of the corneal reflex.

The criticism might be made that, since hypnotics are being considered, the appearance of sleep should be a criterion of efficiency. However, it was found that there is no good method of determining when a rabbit has gone to sleep. The drug manifests itself by first causing paralysis of the hind legs with loss of motor reflex. This paralysis progresses to the front legs and last of all to the neck and head. At this last stage of narcosis the animal is prostated. The next stage is loss of consciousness and the animal is apparently in a deep coma with abolition of all reflexes. It was, therefore, concluded that only the minimum anesthetic doses, if they could be accurately determined, would serve as a comparison for efficiency.

The duration of narcosis also gives interesting comparisons. In the table below, the time is given in hours.

	Orally.		Intraperitoneally.	
	Limits.	Usually.	Limits.	Usually.
Barbital	10–27	18	12–24	16
Phenobarbital	12–30	17	11–27	17
Amytal	4–24	16	3–18	4
Dial	8–24	16	4–16	15
Neonal	12–36	16	4–15	12
Pentobarbital	4–18	15	1–2	1.5
Phanodorn	2–19	12	0.75–2	1.5

It is plainly evident from these figures that the average duration is about the same for all of the drugs studied when given by mouth. However, it was noted that amytal, barbital and neonal in sub-lethal doses sometimes produced narcosis lasting as long as thirty-six hours, with a subsequent general paralysis for as much

as ten hours. Pentobarbital and phanodorn by injection are characterized by producing the shortest period noted, and recovery after administration with these two drugs is more rapid than with the others.

It is thought that the period or duration of anesthesia is not a criterion of efficiency because sometimes the more rapidly acting drugs produce a deeper narcosis than the others. In addition the anesthesia was marked by shallowness of respiration and greatly diminished heart beat, although the animal recovered very quickly nevertheless.

A few other observations of interest are also herewith noted.

Excessive diuresis and constant evacuation of the colon was observed after barbital.

Two animals died two weeks after apparent recovery from dial. Autopsy of the animal revealed nothing abnormal in the intestinal organs. There was noticed a degeneration of the bones in the hind legs, which appeared as a rotting of the shaft and articulating surfaces. This condition was observed only twice with dial and not at all with the other drugs, and probably had no relation to the hypnotic.

Upon autopsy of animals that had died from lethal doses of neonal, there was observed a greatly distended bladder containing a large amount of white deposit. Microscopical examination of the deposit revealed nothing but a few epithelial cells. No barbiturate could be identified in the material, but an examination showed the presence of alkali phosphate. It was concluded that the deposit was mainly this phosphate and of no pathological importance.

By intraperitoneal injection of pentobarbital there was produced very deep anesthesia which lasted from one to two hours. Recovery was very rapid.

A short period of hyperexcitability just after injection of phanodorn was noted.

Recovery from large doses of phenobarbital is comparatively slow. Paralysis after anesthesia may persist in some cases for as long as twenty-four hours.

SUMMARY.

The toxicity in rabbits and the comparative efficiency were studied for amytal, barbital, dial, neonal, pentobarbital, phanodorn and phenobarbital, using both oral and intraperitoneal routes.

Some of the figures for the minimum lethal dose differ markedly from those found in the literature.

Apparently the general ratio of efficiency to toxicity is approximately the same for the seven compounds, except that amytal and pentobarbital seem to be extremely safe by oral administration.

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"A vigorous appeal to Japan, asking her to stamp out the wide-spread illicit opium traffic engaged in by her subjects, has been made in a resolution of the opium advisory committee of the League of Nations. This action followed the assailing of Japan's laxity toward the bootleg narcotics traffic, made by spokesmen for China, England, Canada and the United States."

MONARDA PECTINATA, NUTT., A PHYTOCHEMICAL STUDY.*,[1]

BY JOSEPH B. BURT.

I. The Herb.

A. WEIGHT OF THE PARTS OF THE PLANT.

About four and one-half pounds of the dried herb, which had been collected in Scottsbluff County, western Nebraska, and identified by Prof. J. E. Weaver, of the Department of Botany of the University of Nebraska, as *Monarda pectinata*, Nutt., were carefully separated into flowers, leaves, stems and roots. The weights of the air-dried materials are tabulated below. Inasmuch as most of the plants were devoid of roots, the percentages of the above ground components were recomputed because the results revealed a truer relationship.

Part.	Weight.	Percentage of: Total Weight.	Above Ground Portion.
Flower	759 Gm.	39.4	41.5
Leaf	498 Gm.	25.8	27.3
Stem	569 Gm.	29.5	31.2
Root	102 Gm.	5.3	...
	1928 Gm.	100.0	100.0

B. DETERMINATION OF MOISTURE.

The water content of the air-dried materials was determined by means of the xylene method (1), duplicate determinations being made. The percentage results are tabulated below.

	A.	B.
Flower	8.0 per cent	8.0 per cent
Leaf	8.6 per cent	8.6 per cent
Stem	8.2 per cent	8.2 per cent
Root	6.5 per cent	6.5 per cent

C. EXTRACTION WITH SELECTIVE SOLVENTS.

For the sake of a general comparison with the extractives of the two species of *Monarda* previously examined, the several parts of the plant were exhausted with selective solvents according to the modified Rosenthaler method (2) as employed by Harwood (3) in his study of *Monarda fistulosa* L. A Soxhlet extractor was employed for the petroleum ether and ether extractions. For alcohol, hot extraction in a flask connected with a reflux condenser was used. The aqueous, alkaline and acid extractions were also hot. The alkali was 0.2 per cent potassium hydroxide and the acid 1.0 per cent hydrochloric acid. The differences in the weights of the fully extracted marcs (with all six solvents) and the weights of ash are reported as crude fibre. No correction has been applied for the weight of alkali accumulated in the alkaline extractives, which causes this value to assume disproportionate percentages in some instances, especially in the extraction of the root. In this

* Scientific Section, A. Ph. A., Portland meeting, 1935.

[1] A portion of a thesis submitted to the Graduate School of the University of Wisconsin in partial fulfilment of the requirements for the degree of Doctor of Philosophy. (Pharmacy as major.)

case, on account of the hygroscopic effect of the alkali, it was found necessary to neutralize the alkali with dilute hydrochloric acid before the extracts could be brought to dryness. The solvents were used successively in the following order: petroleum ether, ether, hot alcohol, hot water, hot aqueous alkali and hot aqueous acid. The determinations were carried out in triplicate, but in order to conserve space and at the same time afford a more ready means of comparison, the averages of the three determinations only are reported for each of the four parts of the plant. The percentages of moisture in the air-dried materials are also included in the table which follows:

	Flower, Per Cent.	Leaf, Per Cent.	Stem, Per Cent.	Root, Per Cent.
Petroleum Ether	3.27	6.76	0.65	1.21
Ether	1.55	1.83	0.53	0.52
Alcohol	7.79	9.70	5.19	5.33
Water	17.62	19.78	11.75	11.24
Alkali	39.45	17.68	28.71	69.32
Acid	9.20	13.73	9.67	6.35
Crude Fibre	18.23	10.20	42.28	33.20
Ash	2.32	4.23	0.53	1.27
Moisture	8.00	8.60	8.20	6.50

An examination of this table leads to a few observations which are significant. The relatively small proportions of petroleum-ether and ether-soluble extractive in the stem and root as compared with those of the flower and leaf are especially striking. It was noted in the examination of the xylene used in the determinations of moisture, that those portions used upon the stem and root were free from carvacrol or thymol, as determined by the Flueckiger test, while the portions used upon the flower and leaf gave positive tests. Again, the relatively high values for crude fibre in the stem and root are also noted, as well as the correspondingly low values for ash in these portions of the plant. Variations in the alkali extractives are doubtless of less significance, for the reason that the proportion of alkaline solution required to exhaust the several parts of the plant is not in strict ratio to the weight of sample used, giving rise to a lack of uniformity in the results, due to the unequal accumulation of the alkali in the extracts.

D. ASH DATA.

1. Flower.—The air-dried flowers yielded the following percentages of ash, in two determinations:

	A, Per Cent.	B, Per Cent.
Water-soluble ash	4.41	4.59
Water-insoluble ash	8.47	8.65
Total ash	12.88	13.24

The water-insoluble ash resolved itself into:

	A, Per Cent.	B, Per Cent.
Acid-soluble ash	4.90	4.80
Acid-insoluble ash	3.57	3.85

2. Leaf.—Two determinations of the air-dried material yielded the following results:

	A, Per Cent.	B, Per Cent.
Water-soluble ash	3.76	3.94
Water-insoluble ash	11.53	11.49
Total ash	15.29	15.43

The water-insoluble ash was constituted as follows:

	A, Per Cent.	B, Per Cent.
Acid-soluble ash	6.27	5.90
Acid-insoluble ash	5.26	5.59

3. Stem.—Ash determinations of the air-dried material yielded the following results:

	A, Per Cent.	B, Per Cent.
Water-soluble ash	4.33	4.54
Water-insoluble ash	3.43	3.48
Total ash	7.76	8.02

The water-insoluble ash gave the following results:

	A, Per Cent.	B, Per Cent.
Acid-soluble ash	2.85	2.91
Acid-insoluble ash	0.58	0.57

4 Root.—The air-dried material gave, for two samples, the following percentages:

	A, Per Cent.	B, Per Cent.
Water-soluble ash	2.14	2.08
Water-insoluble ash	2.74	3.17
Total ash	4.88	5.25

The water-insoluble ash resolved itself into:

	A, Per Cent.	B, Per Cent.
Acid-soluble ash	1.79	2.01
Acid-insoluble ash	0.95	1.16

For the purpose of comparison, the ash data given above are retabulated in the following, the averages of the two determinations being reported.

	Per Cent in:			
	Flower.	Leaf.	Stem.	Root.
Water-soluble ash	4.50	3.85	4.43	2.11
Water-insoluble ash	8.56	11.51	3.45	2.95
Total ash	13.06	15.36	7.88	5.06
Acid-soluble ash	4.85	6.08	2.88	1.90
Acid-insoluble ash	3.71	5.43	0.58	1.06

E. INORGANIC CONSTITUENTS OF THE ASH.

The methods followed in the analysis of the constituents of the ash were the same as those employed by Harwood (4) in his study of the inorganic constituents of *Monarda fistulosa*, L. The Cl, CO_3 and SO_4 radicals are reported for the water-soluble ash, and Ca, Mg, Al, Fe and SiO_3 for the acid-insoluble ash.

1. *Flower.*—The following results were obtained from duplicate samples:

	Per Cent.	Per Cent.
Ca	0.35	0.35
Mg	0.20	0.20
Fe	0.34	0.34
Al	1.15	1.13
Cl	0.31	0.29
CO_3	3.21	3.21
SO_4	0.64	0.59
SiO_2	0.43	0.43
Undet.	6.25	6.61

2. *Leaf.*—The following ash constituents were determined:

	Per Cent.	Per Cent.
Ca	0.29	0.36
Mg	0.19	0.20
Fe	0.27	0.27
Al	1.12	1.25
Cl	0.44	0.44
CO_3	2.92	2.94
SO_4	0.49	0.61
SiO_2	0.62	0.65
Undet.	8.95	8.71

3. *Stem.*—The quantitative analysis of the ash yielded the following percentages, computed with reference to the air-dried material:

	Per Cent.	Per Cent.
Ca	0.93	0.96
Mg	0.08	0.07
Fe	0.07	0.08
Al	0.57	0.54
Cl	0.33	0.35
CO_3	2.97	3.00
SO_4	0.50	0.46
SiO_2	0.10	0.10
Undet.	2.20	2.46

4. *Root.*—The following constituents were determined quantitatively, computed with reference to the air-dried material:

	Per Cent.	Per Cent.
Ca	0.24	0.23
Mg	0.15	0.12
Fe	0.20	0.20
Al	0.37	0.37
Cl	0.07	0.07
CO_3	1.82	1.82
SO_4	0.11	0.10
SiO_2	0.09	0.10
Undet.	1.83	2.24

In the tabulation which follows, the percentages of elements and radicals were computed with reference to absolutely dry material, for any conclusions that may be drawn from these figures should be directly comparable and not subject to cor-

rection by the differences in the moisture contents of the several air-dried materials. The values recorded are the averages of the two determinations previously reported.

	Per Cent in:			
	Flower.	Leaf.	Stem.	Root.
Ca	0.43	0.35	1.02	0.26
Mg	0.22	0.22	0.09	0.14
Fe	0.37	0.30	0.09	0.21
Al	1.24	1.29	0.60	0.40
Cl	0.33	0.48	0.37	0.07
CO_3	3.49	3.20	3.25	1.95
SO_4	0.66	0.60	0.52	0.12
SiO_2	0.47	0.70	0.11	0.11
Undet.	6.99	9.67	2.44	2.16

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THE COMPARATIVE ANTISEPTIC ACTION OF OINTMENTS AND RELATED PRODUCTS.*

BY ARTHUR H. BRYAN.[1]

INTRODUCTION.

Using modified Reddish and U. S. P. H. "Cup and Smear" methods with clinical observations wherever practicable, an attempt was made to study the bactericidal activity of 80 well-known U. S. P., N. F., N. N. R., proprietary ointments, face and dental creams.

METHOD.

In the laboratory tests, blood serum heart infusion agar with human, sheep and bovine blood serum was used after sterilization through a Berkfeldt filter.

The first bacterial test organism experimented with was a 24-hour old culture of *Staphylococcus aureus* incubated at 37° C.; later pyogenic cocci obtained directly from acne and pimples pus was cultured.

Intermittent sterilization of the culture media was carried out in an autoclave at 120° C. for half an hour on two or three successive days in individual test-tubes containing 15 cc. of heart infusion agar. After the agar was cooled to 45° C., the sterile blood was added together with one drop from a sterile hypodermic syringe containing a 24-hour old culture of the test organisms. The tubes were well shaken and quickly poured into previously sterilized, wrapped petri dishes.

The varying consistency of the test ointments and other preparations used made them awkward to handle, especially in the small quantities necessary for the

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* Scientific Section, A. PH. A., Washington meeting, 1934.

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test; therefore, the ointments were heated slightly to semifluid state in order to get full surface contact with the agar. It is doubted whether or not this heating interfered with the antiseptic action of the ointment, because ointments that could be used unheated gave identical results with those slightly heated; and, as a further check, one batch of ointments was run unheated using the U. S. P. H. technique as a control. In the Reddish[1] cup method, reasonably equal amounts of ointment were used in the tests by knocking out the ends of glass Luer's syringes, drawing up a definite quantity of ointment and finally smoothing off the surface with a spatula. The outside of the syringe was slightly heated, so that the ointment would run sufficiently for it to be carefully directed and dropped into the cup.

In the "smear" method, previously calibrated 8-mm. bore glass tubes were used as pipettes and plunged down into the test ointments up to a definite mark, and then slightly heated so that the ointments just ran out. The melted ointment was then directed to the center of the agar plate previously inoculated with the pus producing staphylococci. Simply smearing on the ointments with sterile glass stirring rods proved satisfactory provided quantitative tests were not needed.

Another scheme, giving uniform results, which tallied with the results obtained using the naked unheated ointments, consisted in putting all the ointments in separate test-tubes and numbering them consecutively. The test tubes containing the ointments were then heated in hot water at a temperature of not over 45° C. according to the respective melting points of the bases, and shaken thoroughly. Then using an individual piece of 8-mm. marked glass tubing for each test-tube, a definite quantity of the ointment was dropped into the cup or smeared over the surface of the agar as before. Heating greatly facilitated the quantitative handling of the majority of different preparations tested. It also brought the ointments to suitable consistency needed for the "cup" and "smear" methods. The cup method was best for lard base ointments and any other preparations that tend to soften at room temperature. The smear method was finally adopted for all other ointments. After the culture media hardened in the petri dishes, the cup was cut by pressing a test-tube down to the bottom of the media, and the center lifted out with a toothpick or spatula. The usual few drops of liquid culture media were dropped into the bottom of the cup so that diffusion could take place on the floor of the cup.

Sets of smear plates were run with ointment placed above and then below the agar with results fairly uniform in both cases. After a 24-hour period of incubation at 37° C. and one batch at room temperature, the inhibition zones were measured, and the plates photographed or blue printed.

CLINICAL OBSERVATIONS.

1. The characteristic lesions of follicular dog mange and ring worm responded to severe inunctions of iodine and the stronger mercurial ointments, used in veterinary practice, but failed to respond when old ointments were used.

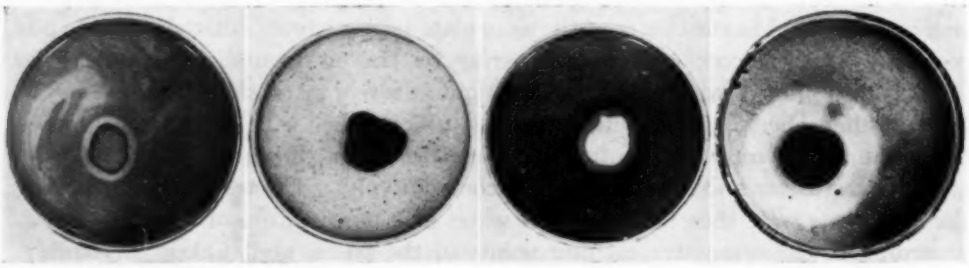
2. The erythematous, desquamative areas characteristic of Dhobie itch responded promptly to inunctions of fresh 10% salicylic acid ointment, the lesions disappearing after a few daily treatments. The local action of the ointment is indi-

[1] Reddish, G. F., Jour. A. Ph. A., 16, 502 (1927).

cated to the patient by a few minutes of intense smarting. When old 10% salicylic acid ointment was used there was no smarting and the lesions did not disappear.

SUGGESTED STANDARD FOR THE GERMICIDAL COEFFICIENT OF OINTMENTS.

The phenol coefficient of liquid antiseptics is the standard for determining the germicidal activity of antiseptics and disinfectants. It is suggested that a similar tentative germicidal coefficient standard be adapted for the testing of the antiseptic strength of ointments and related products. The most satisfactory test for ointments is the Reddish U. S. Public Health Cup and Smear method, with the mercurial ointments giving the most uniform results.



1. 5% Salicylic acid ointment in Benzoinated Lard with inhibition zone of 2.5 mm. in a culture of *Staphylococcus aureus*.

2. Zinc oxide ointment with no zone of inhibition suggesting absence of germicidal activity.

3. 10% Phenol ointment in petrolatum with an inhibition zone of 2.0 mm. against pure cultures of combined *Staphylococcus aureus* and *albus*.

4. Ammoniated mercurial ointment in lanolin base with 8-mm. zones of inhibition and well-marked diffusion. The germicidal activity was well marked against pyogenic mixed infection bacteria taken from abscess pus.

When running Reddish ointment or related products tests it would be well to include for comparative purposes either citrine or ammoniated mercurial ointment or both, for that matter. Measure the width of the inhibition zones of the other products to be tested and make a comparative ratio with the above mercurial ointments. On our tests, citrine and ammoniated mercurial ointments gave approximately 8-mm. zones under varying test conditions, although the U. S. P. H. rated them lower. In order to find the mercury ointment coefficient of any ointment or related product, it is only necessary to divide the test ointment inhibition zone by the mercurial ointment zone, which in this case was 8.

Example: Iodine Ointment gave an inhibition zone of 6.5, then $6.5 \div 8 = 0.81$, which would be the mercury coefficient of the U. S. P. Iodine Ointment.

40 MERCURY OINTMENT COEFFICIENTS.

Citrine Ointment, N. F.	1.2
Ammoniated Mercury Ointment, U. S. P.	1.0
Iodine Ointment, U. S. P.	0.81
Salicylic Acid Ointment, Benzoinated Lard, 10%	0.81
Phenol Benzoinated Lard, 10%	0.81

Mercurochrome, Lanolin and Petrolatum, 2%	0.81
Yellow Oxide of Mercury Ointment, 5%	0.75
A Stainless Iodine Ointment (proprietary product)	0.75
Argyrol Ointment, 10%	0.75
Stronger Mercurial Ointment, U. S. P.	0.7
Red Oxide of Mercury, N. F.	0.65
Mild Mercurial Ointment, U. S. P.	0.6
A Dental Cream (proprietary product)	0.6
Salicylic Acid Ointment, Benzoinated Lard, 5%	0.55
A Dental Cream (proprietary product)	0.5
Phenol Ointment in Petrolatum, 10%	0.5
Phenol Ointment in 75% Petrolatum and 25% Anhydrous Lanolin, 5%	0.5
Tar Ointment	0.37
Calamine Ointment	0.37
Alcoholated Sulphur Ointment	0.37
Stimulating Ointment	0.34
Phenol Benzoinated Lard, 10%	0.32
Thymol Iodide Ointment	0.3
Tannic Acid, Belladonna, Camphor, White Precipitate, 3 yrs. old	0.15
Yellow Oxide of Mercury, Ophthalmic, 1%	0.15
Phenol in Petrolatum, 5%	Zero
Phenol in Anhydrous Lanolin and 5% Yellow Wax	"
A Face Cream (proprietary product)	"
Zinc Oxide Ointment	"
Chrysarobin Ointment	"
Boric Acid Ointment, 10%	"
Acriflavine, Lanolin Base, 1%	"
Sulphur Ointment	"
Compound Resorcin	"
Methylene Blue, Lanolin, 2%	"
Gentian Violet, Lanolin, 2%	"
Ichthyol Ointment	"
Iodoform Ointment	"
Boric Acid, Petrolatum and Lanolin, 5%	"
Precipitated Sulphur Ointment	"

This substantiates the work of Husa, showing that the incorporation of yellow wax reduces the antiseptic properties of phenol ointments to zero.

CONCLUSIONS DRAWN FROM LABORATORY OBSERVATIONS.

1. Lanolin and Benzoinated Lard appeared to be the most satisfactory bases for maximum antiseptic and diffusion activity.

2. U. S. P. and N. F. ointments showed no antiseptic action in strengths of 0.05% to 1% as indicated by the absence of inhibition zones, except opthalmic yellow oxide of mercury ointment, which gave a uniformly good zone of inhibition.

3. The recently prepared U. S. P. and N. F. ointments, in which the active ingredient content was 5% and 10%, that were tested showed antiseptic action as shown by well-defined inhibition zones, except 5% phenol in petrolatum. Phenol in a mixture of lanolin and petrolatum, according to Professor Husa's formula, gave good inhibition zones. Five per cent ointments gave 3–4-mm. zones; and 10% showed 7–8 mm., including twice the antiseptic strength.

4. Tar ointment, all the mercurials, including mercurochrome, argyrol, gentian violet, salicylic acid, iodine, showed consistent antispetic action with well-defined zones of inhibition under all test conditions.

5. The largest and most consistent inhibition zones were formed with the various iodine and mercurial ointments; two per cent mercurochrome and 2% mercuric iodide ointments showing the widest areas of diffusion and inhibition.

6. Mercurial ointments did not deteriorate over a period of ten years, all showing standard inhibition zones comparable to fresh ointments. The other ointments apparently showed decreased antiseptic activity with lessened or no inhibition zone on standing.

7. The rate and extent of diffusion was evidently influenced by such physical characteristics of the base as melting point, surface tension, permeability, cohesion and adhesion, etc., as indicated by varied zones obtained with the same medicaments in different bases, and under altered laboratory conditions.

8. U. S. P., N. F. and proprietary iodine, phenol and salicylic acid ointments gradually lost their antiseptic action within 3–9 months, the iodine in petrolatum base showed least deterioration. U. S. P. iodine ointment on March 1934 gave a 6.5-mm. inhibition zone and on November 1933, the inhibition zone was only 1.4 mm. Thus four months' standing evidently decreased the antiseptic activity of the ointment.

9. Ointments, such as boric acid 10%, acriflavine, methylene blue, icthyol, zinc oxide, compound resorcinol, chrysarobin, sulphur, etc., showed no inhibition action on staphylococci, mixed pyogenic cocci or subtilis cultures. Zinc oxide showed a very faint indefinite linear zone around the ointment periphery.

10. In contrast to the comparative bactericidal inertness of sulphur ointment the alcoholated sulphur ointment and sulphur iodide ointment showed antiseptic action depending upon the base and the amount of alcohol or iodine incorporated therein.

11. The mercurial ointments, irrespective of whether half or full strength, showed practically equal widths of the inhibition zones. However, the diffusibility of both tends to be the same; therefore this result does not necessarily mean equal antiseptic activity.

12. Inhibition zones were wider on staphylococcic and streptococcic than subtilis cultures. Other spore-bearing air flora grew outside but not within the inhibition zones.

13. The most uniform results were obtained when the ointments were freshly prepared and smeared on either unheated or slightly heated. Overheating gave confused and even negative results, in some instances, probably due to chemical action resulting in stearification, with the fatty esters, inactivating the preparations.

14. The diffusion and inhibition zones on the plates remained after several months' standing. Some old plates with good inhibition zones were purposely exposed to air-bacterial flora. There was no growth within the inhibition zone, showing that the antiseptic action was still there.

15. Most commercial face creams showed no bactericidal activity with absence of inhibition zones on plate cultures of pimple and acne pus bacteria.

16. Of well-known dental creams only two showed marked inhibition zones indicative of antiseptic activity.

17. The iodine, phenol, argyrol and salicylic acid ointments showed the greatest tendency to deteriorate as evidenced by decreased or lost inhibitory powers.

18. In general epidermatic ointments appeared to show less activity than endermatic or diadermatic ointments. This hypothesis is exemplified by the phenol and salicylic acid in petrolatum results.

19. The Reddish "Cup and Smear" method proved useful for testing the comparative antiseptic strength of ointments, face creams, salves and also dentifrices.

SUMMARY.

This study indicated the necessity for preparing and dispensing fresh ointments because, aside from the mercurial ointments, all others tend to undergo deterioration on standing.

The *Australasian Journal of Pharmacy* quotes:

"The United States Federal Trade Commission is objecting to the use of the words 'laboratory' or 'laboratories' in the name of an organization unless the firm does actually maintain laboratories for the purpose of manufacturing or compounding the preparations that it distributes. The Commission is of the opinion that such representations constitute an unfair trade practice, and manufacturers are being asked to desist from using this title unless they are in a position to comply with the requirements laid down by the department."

FURTHER PIGEON BIOASSAYS AND DIURETIC TESTS OF DIGITALOIDS.*

BY A. J. LEHMAN.[1]

Pigeon assays of a number of the more important and acceptable digitalis specialties were reported in a previous paper (1). The introduction of some new products and of a diuretic test (2) since that time made it desirable to bring assays and comparisons with the pigeon method up-to-date; hence, the present report.

METHOD AND PRODUCTS USED.

The pigeon assay for emetic doses was carried out according to the original description of the method (3), the number of pigeons varying according to requirements. The number ranged from 18 to 73; average, 38 birds for each assay. Intravenous fatal doses were determined in the same pigeons used for emetic doses, after a period of recovery. Selection of pigeons for elimination of a conditioned vomiting reflex was not practiced as it was unnecessary. Such selection has been practiced by Lieb and Mulinos (4), and a slow intravenous injection, as in the cat method, by Haag and Woodley (5), with results which confirm the value of the pigeon method for bioassay of digitalis. The great advantages of the pigeon emetic method have been summarized as follows by Hanzlik (6), who introduced the method: simplicity, reasonable accuracy and economy; pigeons are easily available everywhere at any time; no surgical anesthesia or operation is necessary; a result is obtained in 15 minutes; pigeons can be used repeatedly; fatal dose can be obtained in the same pigeon after the emetic dose; results compare favorably with the cat method; the probable full therapeutic dose can be estimated from the pigeon emetic dose. The emetic and fatal doses of, and other doses for comparison with, the products tested in this study are presented in Table I.

A total of 5 digitaloid principles and 1 purified (fat free) tincture of digitalis were assayed. The purified principles were verodigen, glucosides of *Digitalis lanata*, digoxin (also from *D. lanata*), urginin and thevetin. These were used in solutions as supplied by the manufacturers; verodigen being prepared as a 1:1000 solution. Digiglusin, which is claimed to be a fat-free tincture of digitalis, was used in dilution according to the pigeon method. None of the products is described in N. N. R., but urginin is a Council-accepted product. The doses used in this paper indicate mg. or cc. of product for each Kg. body weight of pigeon.

TABLE I.—COMPARATIVE DOSES OF DIGITALOIDS.*

Digitaloid.	Pigeon. M. Em. D.	Pigeon. M. F. D.	Ratio, M. Em. D. / M. F. D.	Predicted Total Clinical Dose.	Full Therapeutic Dose Claimed.	Cat, M. F. D.
Digitalis lanata	0.05 mg.	0.3 mg.	6.0	3.0 mg.	1.75 mg. (19)	0.34 mg. (16)
Urginin	0.10 mg.	0.45 mg.	4.5	6.0 mg.	3 to 9 mg. (18)	0.2 mg. (18)
Digoxin	0.12 mg.	0.35 mg.	2.9	7.2 mg.	3.0 mg.	0.44 mg. (15)
Thevetin	0.31 mg.	1.4 mg.	4.5	18.6 mg.	8.5 to 25.5 mg. (14)	0.85 mg. (13)
Verodigen	0.37 mg.	1.0 mg.	2.7	22.4 mg.	6.5 mg. (17)	0.65 mg. (17)
Digiglusin	0.25 cc.	1.1 cc.	4.4	15.0 cc.		

* M. Em. D. = minimum emetic dose; M. F. D. = minimum fatal dose; mg. = milligram; cc. = cubic centimeter; digits in parenthesis indicate references to papers listed at the end of the paper.

EMETIC AND FATAL DOSES.

All of the digitaloids used caused emesis. Table I shows that doses for emesis varied considerably. The *Digitalis lanata* glucosides had the lowest emetic dose, or, 0.05 mg., and verodigen

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the highest, or 0.37 mg. The doses of the other products fell in between these two and were actually as follows: thevetin, 0.31 mg., digiglusin, 0.25 cc., digoxin, 0.12 mg. and urginin, 0.1 mg.

From these results it would appear that verodigen might be preferable for therapeutic use owing to the comparatively larger dose required to provoke emesis. However, this would not follow, since the fatal dose of verodigen was relatively low, although second highest. This indicates that its emetic and cardiac actions are relatively weak, and the margin of safety in therapeutic usage, as judged by the lowest emetic-fatal dose ratio, rather narrow. The *Digitalis lanata* glucosides, claimed to be a pure, natural mixture of digilanid A, B and C, would be the safest according to the same criteria, since the emetic dose was only one-sixth the fatal dose, although they were more efficient than verodigen according to both the emetic and fatal doses. Although the emetic and fatal doses of digoxin, which is a glucoside of *D. lanata*, urginin and thevetin varied among themselves, the ratios of these doses were practically the same, namely, 4.4 to 4.5, which was next to the highest ratio, or 6, for *Digitalis lanata* glucosides. These high ratios compare favorably with those of good strong leaves of *Digitalis purpurea* (3) and indicate satisfactory safety margins in therapeutic use.

The cause of the widely differing ratios of emetic and fatal doses for weak and strong products of digitalis is not known. One possibility, namely, impurities, may be ruled out, since the relation apparently holds with pure glucosides as well as with specially prepared products, and the ordinary official tinctures of digitalis. The contrasting tendencies in killing powers of the digitalis glucosides should not be overlooked, for dangerous symptoms may not be suspected from the relatively minor toxic effects such as nausea or emesis. The latter should be a sign for stoppage of the medication, keeping in mind that with some digitaloids the fatal dose may not be far away, such as those with a low emetic-fatal dose ratio.

COMPARATIVE FATAL DOSES.

Some comparisons were made with intravenous fatal doses in pigeons and cats the latter being obtained from reports in the literature. Table I shows that the fatal doses in pigeons and cats were close for digoxin only. The fatal doses of the following were decidedly higher in pigeons: Verodigen, about 20 per cent, thevetin, about 70 per cent, and urginin, over 50 per cent. Accordingly, cats would appear to be more sensitive than pigeons, but it must be remembered that the procedures of administration are not always identical, especially the rate of injection and spacing of doses. The cat and pigeon fatal doses in this report are not as comparable as those for *Digitalis purpurea* in a previous report (3).

The symptoms of poisoning from the digitaloids were indistinguishable from those from digitalis specialties or tincture of digitalis. While the potency and fatal doses varied considerably, the killing power of the weaker products was, in general, out of proportion to the emetic efficiency, confirming previous results with ordinary digitalis (3). Consequently, these digitaloids have no special advantage over the ordinary official preparations except for the injection feature which may be useful in special cases.

COMPARATIVE CLINICAL DOSES.

As for use of the pigeon emetic dose for predicting the probable full therapeutic or clinical dose, Stockton (7) has shown by clinical tests that this is practically fea-

sible for digitalis. Guidi (8), Starnotti (9), Carratalá (10) and Redonnet (11), who have made similar comparisons, practically agree with Stockton's experience, except for interpretation of minor details. Dock, Stockton and Lehman (12) have made comparisons with results of other methods and confirm the close parallel of pigeon emetic and clinical effects. No clinical comparisons of the digitaloids of this report have been made in this institution, but the full therapeutic doses claimed for them in the literature are presented in Table I. These may be compared with the clinical doses predicted from the pigeon emetic doses for a 60-Kg. man, using the product according to the Eggleston method of medication. The doses claimed in the literature may not have been determined according to the latter method. It is seen that only the predicted and claimed clinical doses for urginin and thevetin might agree, provided averages of the claimed dose-ranges be used. Digoxin, according to pigeon estimates, would permit a clinical dose over two times that claimed, *Digitalis lanata* glucosides, not quite two times and verodigen, over three times. Further discussion is hardly worth while, since the methods and conditions of administration may not be exactly comparable.

EFFECTS ON URINE FLOW.

Defandorf (2) has recently described a diuretic (oliguric) test on the cat for bioassay of digitalis. It appeared interesting to make some comparisons with effects on urine flow in pigeons. Three different types of products were tested, namely, a tincture of digitalis prepared according to the official method, digitan tincture (Merck) and digoxin. The emetic doses of these products were determined previously, and then their effects observed on urine flow following repeated intravenous injections of one-quarter the emetic dose every five minutes until death.

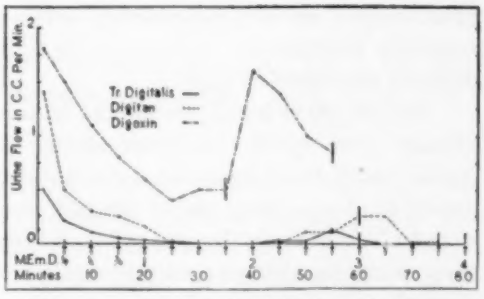

Fig. 1.—Effects of digitalis, digitan and digoxin on the urine-flow in pigeons. M. Em. D. = minimum emetic dose, each arrow indicating an additional one-quarter the emetic dose. A short vertical line on a curve indicates death of a pigeon.

The pigeons were anesthetized with pentobarbital, using 25 mg. per Kg. intramuscularly. Blood pressure records were obtained from the carotid artery in the usual manner. Both ureters were catheterized with slender glass cannulas and joined by means of a Y-tube so that urine flow from both kidneys was obtained simultaneously. Diuresis was encouraged by administering 20 cc. of 0.9 per cent sodium chloride solution by vein, and, when the flow of urine became constant, a control flow was taken for 5 minutes. The digitalis solution was then administered so diluted with physiological salt solution that 1 cc. contained 1 M. Em. D. Urine flow was measured constantly throughout each experiment. The average results from 2 pigeons each for the 3 products tested are presented in Fig. 1.

It is seen that the first dose of each product caused an immediate decrease in urine output. This decrease became more marked with each succeeding dose until one and one-quarter emetic doses were reached when the urine flow ceased altogether, or dropped to its lowest point, depending on the initial magnitude of diuresis. When a total dose of one and three-quarters emetic doses was reached with digoxin, and two and one-quarter doses with digitalis and digitan, the urinary output suddenly increased for the next few doses and then gradually declined as death ap-

proached. That this sudden increase in urine output was not due to the fluid injected was demonstrated by negative effects in one pigeon each, on digitan and digitalis, from injections of 10 cc. per Kg. of 0.9 per cent sodium chloride solution during the period of anuria.

There was no correlation between the blood pressure and the urine flow. The first emetic dose generally produced a small rise in blood pressure followed by recovery, and thereafter there were slight fluctuations either above or below the control level. During the period of anuria the blood pressure was above the control level in one-half the pigeons. At no time were the changes significant, and sudden collapse to the zero level occurred only when the full fatal dose was reached. Obviously the effects on urine flow could not be attributed to a failing circulation, but they were probably the result of a marked renal vasoconstriction. Such results would be expected in normal individuals.

However, in cats, Defandorf reported a marked diuresis after the first dose of digitalis, followed by a decrease, and, as the injection of digitalis was continued, a further reduction to the control or initial flow. Almost all this is in direct contrast to the results on pigeons, which followed closely the anuric effects, if any, in normal human subjects, rabbits or other animals. As is well known, increases in urine output of human subjects occur only in edema and anasarca. Therefore, cats respond abnormally. Or, the variability is so great in these animals that results on urine output are not noteworthy unless a large number of cats is used, which is generally prohibitive. This appears to be another instance of the unreliability of digitalis responses of cats.

On the other hand, the effects on urine flow of the digitalis products tested on pigeons were quite consistent among themselves, and with expectations. Repeated small doses produced a gradual decrease in urinary output which reached its lowest level at a little above the full emetic dose. If such a marked anuric effect were to be chosen as the end-point, it follows that the urinary reaction would be no more sensitive than the emetic end-point, which is distinct and definite. Moreover, the ease and simplicity of carrying out a bioassay according to the pigeon emesis method completely outweighs the more difficult and complicated procedure necessary for accurate determination of urine output. The urine method has nothing to offer as a bioassay method for digitalis, although it might be useful in pigeons for comparing the renal vasoconstrictor efficiency of different products.

CONCLUSIONS.

1. The following 6 new digitaloids were bioassayed by the pigeon method for emetic and fatal doses, and comparisons made with the cat fatal, and full therapeutic doses reported in the literature: *Digitalis lanata*, urginin, digoxin, thevetin, verodigen and digiglusin.

2. Digitalis, digitan and digoxin were found to produce anuric effects in pigeons, in agreement with similar known effects of digitalis in normal human subjects and some other mammals, but in contrast to a diuretic effect claimed for cats, which respond either abnormally or too variably.

3. Urine flow as an end-point for estimating the potency of digitalis products has nothing to offer as a bioassay method, being too variable and unnecessarily complex and difficult, as compared with the easier and simpler pigeon-emesis (alone

or combined with fatal dose) method whose value and applications have been sufficiently established.

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A STUDY OF THE TOXICITY AND ANTIPYRETIC ACTION OF D. GLUCONO-PARA-PHENETIDIN.*

BY HERBERT A. BRAUN AND GEORGE F. CARTLAND.[1]

Within the last decade a number of synthetic modifications of acetphenetidin and acetanilide have been studied in an attempt to increase the antipyretic and analgesic action of these compounds or to reduce their toxicity.

Hambourger[2] has reported pharmacological studies on the gluconic acid derivative of para-phenetidin $C_6H_{11}O_6NHC_6H_4OC_2H_5$. He finds that this compound has a very low toxicity as compared to acetphenetidin when administered orally to rats. He states that, as an antipyretic, it is about as effective as acetphenetidin when administered in equimolecular portions to rabbits which had been fevered with hay infusion.

We have completed a study of glucono-para-phenetidin in which we have confirmed the findings of Hambourger regarding the relatively low toxicity of this compound as compared to acetphenetidin. However, in contrast to Hambourger's report, we found that glucono-phenetidin exerts a much lower antipyretic action in fevered rabbits than that produced by equimolecular quantities of acetphenetidin.

ACUTE TOXICITY.

Glucono-phenetidin was administered as a suspension in 5% acacia to albino rats by means of a stomach tube. Since the quantity of this drug was too great to be administered in one dose, three divided doses were given over a period of three

*,[1] From the Laboratories, The Upjohn Company, Kalamazoo, Michigan.

[2] Hambourger, W. E., *Proc. Soc. Exptl. Biol. Med.*, 31, 365-367 (1933).

hours. The minimum lethal dose (M. L. D.), or the dose which killed more than 50% of the rats, was found to be greater than 50 Gm. per Kg. of rat.

Parallel experiments were conducted to determine the acute toxicity of acetphenetidin. The results given in the table indicate that the M. L. D. for this drug is 2 Gm. per Kg. of rat. The maximum tolerated dose (M. T. D.), or the dose at which toxic symptoms appear, was found to be 0.75 Gm. per Kg. Toxic symptoms observed were cyanosis, slow respiration, depression, loss of equilibrium, coma and finally death.

TABLE I.—COMPARATIVE TOXICITY OF GLUCONO-PHENETIDINE AND ACETPHENETIDIN.

Glucono-phenetidin.			Acetphenetidin.		
Dose per Kg./Gm.	No. of Animals Used.	% Mortality.	Dose per Kg./Gm.	No. of Animals Used.	% Mortality.
20	5	0.0	0.75	2	0.0
30	5	0.0	1	4	0.0
50	5	0.0	2	10	60
			3	10	90
			4	5	100
			5	2	100

By means of spectroscopic examination of the blood of depressed rats, methemoglobin formation could be detected when doses of 1 Gm. per Kg. of acetphenetidin were administered. At no dose of glucono-phenetidin could the presence of appreciable amounts of methemoglobin be determined, indicating that it is quite resistant to destruction in the intestinal tract which accounts for the greatly decreased therapeutic activity of the substance.

ANTIPYRETIC ACTION.

Rabbits were used as experimental animals. They were starved for forty-eight hours and were given no water for twenty-four hours. At the end of this time, the animals were fevered by injecting 10% hay infusion which had been incubated at 37° C. for twenty-four hours. Five cubic centimeters of this infusion per Kg. of rabbit were injected subcutaneously. Normal rectal temperatures were taken at the beginning of the experiment. Two hours were allowed to elapse after the injection of the hay infusion before a second reading was taken. Increases in temperature varying from 0.5°–2° C. over the normal were attained. When the fever temperature was reached at the end of the two hours, the drugs suspended in a 1% acacia solution were administered to the rabbits by means of a stomach tube. Rectal temperatures were taken at hourly intervals during the course of the experiment.

In the majority of the experiments, ten rabbits were used for each trial. From one to three trials were attempted for each dose. Of the ten rabbits used two served as room temperature controls, two as fever controls, three were given acetphenetidin and three glucono-phenetidin. Six doses of the drug were administered. The doses of the first three trials were calculated on the basis of molecular weight, the ratio of glucono-phenetidin to acetphenetidin being 7:4. In the last three trials, 0.75 Gm. per Kg., the dose which was found to give an optimum depression of the temperature for acetphenetidin was compared with multiples of the equimolecular dosage (1.31 Gm.) of glucono-phenetidin.

(1) 0.50 Gm./Kg. of acetphenetidin to 0.87 Gm./Kg. of glucono-phenetidin.
(2) 0.60 " " 1.05 " "
(3) 0.75 " " 1.31 " "
(4) 0.75 " " 2.62 " "
(5) 0.75 " " 5.24 " "
(6) 0.75 " " 10.50 " "

In the first three trials where molecular equivalents of glucono-phenetidin were compared with acetphenetidin administered at 0.50, 0.60 and 0.75 Gm. per Kg., the acetphenetidin was much superior to glucono-phenetidin in causing a depression of the temperature in fevered rabbits. The dosage of 0.75 Gm. of acetphenetidin per Kg. produced an optimum depression of temperature and consequently was chosen as a basis of comparison for higher doses of glucono-phenetidin which were 2, 4 and 8 times the equimolecular dosage. In each case, the antipyretic effect of glucono-phenetidin was less than that of acetphenetidin. In Chart I, the temperature curves of fevered rabbits treated with acetphenetidin 0.75 Gm./Kg. and glucono-phenetidin 10.5 Gm./Kg. are compared with the untreated controls. Each curve represents the average values obtained with five rabbits. Acetphenetidin caused a greater depression of temperature which lasted for more than five hours while the temperature of the fevered rabbits receiving glucono-phenetidin was above normal after two hours.

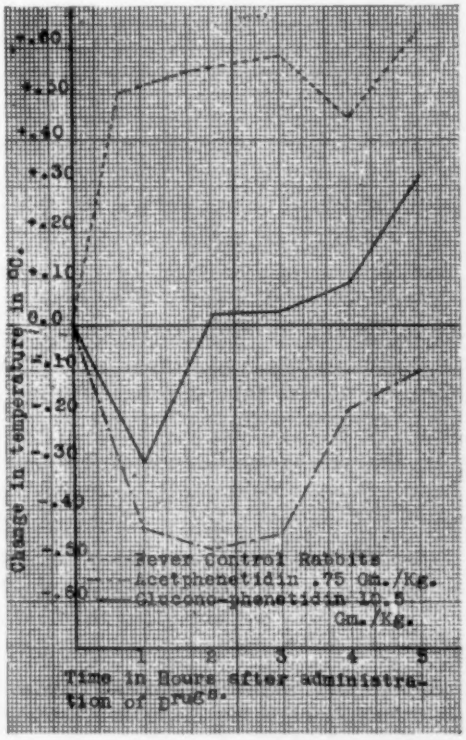

Chart I.

CONCLUSIONS.

(1) A study of the toxicity and antipyretic action of glucono-phenetidin and acetphenetidin has been completed and is described.

(2) Toxicity. Glucono-phenetidin was found to be non-toxic in doses of 50 Gm./Kg. in the rat confirming previous results. The M. L. D. of acetphenetidin was found to be 2 Gm./Kg. of rat which means that glucono-phenetidin is twenty-five times less toxic than acetphenetidin in the rat. The M. T. D. for acetphenetidin is 0.75 Gm./Kg. of rat.

Methemoglobin formation was not observed with glucono-phenetidin but was noted with 1 Gm./Kg. of acetphenetidin.

(3) Antipyretic Action. Acetphenetidin and glucono-phenetidin were not found to be approximately equal when administered on the basis of their molecular weights using the 4:7 ratio. When the dosage of glucono-phenetidin was increased

to eight times that required by this ratio, its antipyretic effect was still less than that produced by acetphenetidin.

The above findings conform with previous conceptions of investigators in the field of antipyretics, namely, that the toxicity and therapeutic activity of antipyretics decrease with an increase in the size of the substituted radical. The most effective compounds have the ethyl or acetyl grouping.

(A Paper of Scientific Section—"A Chemical Study of the Fixed Oil of Poke Root"—Page 636.)

DRUG STANDARDIZATION.*

BY E. R. SERLES.[1]

It is a far cry from our modern conception of rational therapy to the time when the medical code of Hammurabi prescribed that the suffering Babylonians should treat their ills by charm, employing precious stones, frankincense or, what was even worse, the oral administration of lizard's blood, swine's teeth, moisture from pigs' ears, excreta of human beings, animals and even flies.

Yet the toad skin which was used in those days without the slightest inkling of its real merit is to-day known to contain substances which act much like digitalis. Trendelenburg in 1909 isolated toxic principles from the skin of the common toad (Bufanin and Bufotalin) which produced the typical therapeutic effects of digitalis.

Ma Huang, the Chinese plant Ephedra, has been known in Chinese medicine for more than 3000 years, but it remained for Chen and his co-workers to show us its relationship to adrenalin and its superiority to the latter in certain instances.

Bones may not have been judiciously administered during the age of Ptolemy; lizard's blood would hardly be classed as appetizing; yet it is a significant fact that some of our great packing plants can afford to sacrifice the carcasses of their daily slaughter at extremely low figures because of the profits taken from the sale of glandular extracts and preparations made therefrom.

How glibly we jest about the food we eat, asking ourselves about the vitamins it should yield. We may or may not take much stock in the claims made that certain drugs and food products are essential to growth and health and thereby eliminate disease, yet the pharmacist who still urges his customer to try a bottle of some standard blood purifier or the physician who still prescribes strychnine as a heart stimulant is only a shade ahead of the pharmacist who prepared a prescription for Schesch (a queen of the third Egyptian dynasty) which contained equal parts of the heel of an Abyssinian greyhound, of date blossoms and of asses' hoofs boiled in oil, recommending the same for a hair restorer.

The early history of the practice of the "Healing Art" is filled with countless instances of confusion, quackery and jealousy. For hundreds of years suffering humanity was the victim of the charlatan, the knave and superstition.

Gradually the more learned men of science began to break down the severe censorship of church and state and the chaos of knowledge concerning diseases and their treatment took on a more rational aspect.

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This was especially true concerning the selection of drug substances used as remedial agents. The first record of a systematic effort to standardize drugs is found in the writings of Giacomo di'Dondi (1298–1359) who in the latter part of the thirteenth century wrote and secured publication of a treatise on "medicinal plants and simples" known as "Aggregator de Medicinis Simplicibus."

In 1473 the first medical dictionary, "Synonyma Medicinæ" was published at Strassburg. The volume contained definitions of drugs and simples known to the Greek, Latin and Arabic civilizations and was the work of Simone de Cordo who died more than a hundred years before the book was published.

These early works undoubtedly stimulated a more scientific trend of thought toward the use of drugs in the treatment of disease, but it can scarcely be claimed that they did more than to classify a substance as to its source and physical appearance.

To Valerius Cordus, therefore, must go the credit for the compilation and publication of our first Pharmacopœia in the year 1546. The subject matter therein contained was only a review of pharmaceutical formulas considered by Cordus to have unusual merit, yet it was of sufficient import to receive the approval of the Roman Senate, and the local committee of physicians to whom it was referred for examination. The committee reported that in their opinion it was the most complete and accurate treatise of its kind and ordered its publication without revision.

The Senate further ordered that physicians and pharmacists make use of the formulas compiled by Cordus in their respective practice, thus originated the first attempt at drug standardization. The text went through five revisions before 1666 and so great was the demand for the copies that it was published in Paris, Venice, Lyons and Antwerp.

Many works of a similar character were published in other countries and it is interesting to note their effect upon drug cultivation. Drug gardens sprang up almost over night as the artisan sought to supply the demand for the highly recommended medicinal substances. The first garden of this kind was established in Padua, Italy, in 1533.

The first legally controlled formula of all time was established under the British Law in 1673. It was known as "Goddard's Drops" and was purported to be a therapeutic agent of almost divine virtue. It was held to be of such great value as a remedy that Charles II is said to have purchased the right of patent from Dr. Goddard for $25,000.00. Actually the preparation seems to have been only the distillate of human bones diluted with Spirit of Nitre or Spirit of Wine.

This form of drug standardization is still with us to-day and I am sorry to say that the physicians have for the most part continued the practice by seeking "letters patent" upon their favorite prescriptions.

I have no quarrel with the manufacturer or professional man of whatever calling who seeks to protect his property rights in the sale and distribution of a remedial agent which is the result of conscientious scientific endeavor and which through unscrupulous manipulation might fail of its therapeutic value, but I do condemn the system which permits the modification of well-established formulas of known value in order that their producer may write thereon a "new name" and ascribe thereto unreasonable therapeutic values.

Our own Pharmacopœia came into being in January 1817, through the efforts

of Dr. Lyman Spalding when he placed before the Medical Society of the County of New York a project for the formation of a National Pharmacopœia. You are all more or less familiar with the history that surrounded this important event but I doubt if there are many present here to-day who have much of an idea as to how the eleventh revision of this drug standard has been effected.

The first edition of the U. S. P., of which I have a page proof copy, was no very great scientific contribution to the advancement of medical or pharmaceutical knowledge.

The eleventh revision, however, represents the acme of scientific knowledge gathered from the fields of biology, chemistry, physics, medicine and all of the allied branches of applied science throughout the civilized world.

Every remedial agent or substance used in the manufacture of a medicinal preparation which conforms to a U. S. P. title is subjected to rigid standardization. Even water which may be used to prepare a crude drug for further extraction and which is no part of the finished product must contain not more than 0.001 Gm. per 100 cc. of dissolved solid matter.

Every chemical, solution, biological product or diluent must contain the lowest possible amount of inert material and every precaution is taken to guard against deterioration of the finished product.

Many of you may feel that drug standardization is of concern to the pharmacist only, but I assure you it is not. Take, for example, the standardization of Insulin. Before the pancreas gland leaves the slaughtered animal a veterinarian has carefully inspected the carcass, then comes the careful storage, the crude extractions, the countless number of operations it passes through before it is ready to be tested under the supervision of pharmacists and physicians. It is finally ready for the market, but it must still be properly stored lest it become inactive.

Next comes the patient and though it may be clinically evident that he is a diabetic no Insulin should be administered until we know the various blood sugar levels and his carbohydrate tolerance, all of which require the knowledge of a physician and a nurse or laboratory technican. He may even require a dental service, but more important than all of these he will require a daily dosage of an accurately standardized Insulin.

Thus we see that a single patient has, whether we acknowledged it or not, made us professionally interdependent.

Many similar instances might be cited wherein the preparation, standardization and use of a drug require the whole-hearted coöperation of the manufacturer, the physiologist, the chemist, the pharmacologist and the members of every profession here represented, yet there still remain certain practices in medical therapy and drug standardization which are a trial to all of us.

Take, for example, the case of digitalis—when Sir William Withering first gave to the world his knowledge of the therapeutic value of the old time infusion he little dreamed that he would begin a controversy which should last for generations, a controversy which promises to last through generations yet to come.

There are in the United States to-day more than seventeen manufacturers of digitalis preparations each claiming for his special product a certain superiority of therapeutic achievement not common to any other digitalis preparation heretofore produced. True, the drug is and has been officially described in every Pharma-

copœia published for many years. Its therapeutic value has been clearly established by the best means known to science. Its clinical usage is understood by every physician but we are still willing to kid ourselves into thinking we love our wives and sweethearts the more whenever they have a new dress. What I am trying to say is this. Why should we make room for a new medicinal preparation which professedly admits by its own label that it is equal to a certain number of units of strength as prescribed by the U. S. P. if you will but increase or decrease the dosage as suggested by the manufacturer? Why should we crowd the pharmacists' shelves with just one more bottle of a drug which he already has in stock, thus increasing his inventory and the cost to the patient? What special advantage is there in having seventeen different kinds of digitalis preparations all adjusted to the same standard, the administration of which results in approximately the same therapeutic effect?

The chaos in connection with the instance cited is equally true with aspirin, cod liver oil, liver extracts and many other remedial agents now found in the U. S. P.

An even greater sacrilege of scientific knowledge is made by those who combine a few standard U. S. P. drugs, add a flavor or some inert substance and christen the newborn creation with a "gold medal" name. Then they detail the physician or dentist, who in turn hands the new wonder to his patient. When sufficient publicity has been established, the radio advertising begins and in a short time every cross-road merchant has the product for sale.

I need not recite to you the evils of this practice. You know them too well.

In the last quarter of a century we have come far from that time when a knowledge of the "Healing Art" was based upon chicanery, or magic. We have progressed far in the removal of the enigma of professional jealousy which here is evidenced by what I believe is the first time such a convention as this has been held within the confines of the United States, yet I adjure you not to be swallowed up in the complacent satisfaction of a good beginning.

Each succeeding step in scientific progress has been marked by untold labor. There is no place in the Interprofessional program for those who assume the laggard's part or jeer at others' faltering steps.

THE ANTISEPTIC ACTION OF MOUTH WASHES AND TOOTH-PASTES IN VIVO.*

BY ARTHUR H. BRYAN.[1]

Previous attempts to evaluate antiseptics have been largely based on *in vitro* germicidal coefficient determinations, the data coming from the power to kill living bacteria grown in artificial media. The present experiments contemplate a series of *in vivo* observations in an effort to evaluate the effectiveness of mouth washes, tooth-pastes and tobacco smoke, in inhibiting the growth of nasal and mouth flora of pathogenic microörganisms directly in the mouth. The mouth washings of several hundred students were examined bacteriologically over a period of four

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years and statistical tables compiled from the direct germicidal action of the antiseptic mouth washes and tooth-pastes in their mouths.

DISCUSSION.

Bacteriology is not an exact science, and wide ranges of difference in *in vivo* experiments, with daily unaccountable variations in count and flora were met with; nevertheless, general trends were noted with some degree of reliability, especially when results coincided with whole groups of participating students.

METHOD.

Ten cubic centimeters of sterile water were used as a gargle and mouth wash for 1 minute for every student participating in the experiment. At the end of the minute, the mouth wash waters were expelled into sterile test-tubes. Serial dilutions of each wash water were made and plated in ordinary nutrient agar, but in some

Mouth Flora in vivo per cc. of wash water 10 minutes after gargling with the following mouth washes.

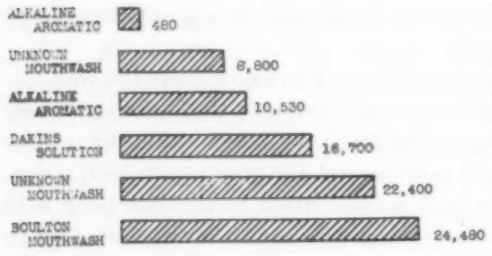

Fig. 1.

Mouth Bacteria.—Average bacterial count of 37 students following the use of the six U. S. P. mouth washes 30 minutes after gargling with them.

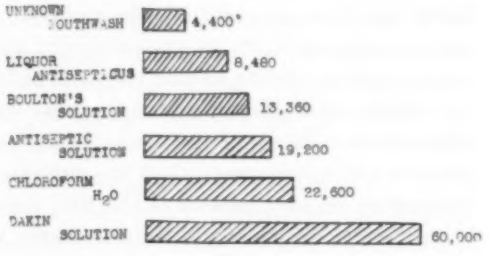

Fig. 2.

experiments blood serum agar was substituted. The plates were inoculated, while the culture media was at 50° C. with the wash water dilution and incubated at 37° C. for 48 hours. The viable mouth bacteria tended to grow out as well-defined colonies at the expiration of that period. Colonies which were small, pin point, or discrete gold or yellow color, were considered as probably pathogenic, while the molds and spreaders were arbitrarily classified as harmless saprophytes. Slides were made of suspicious colonies and simple presumptive determinations made. Each plate was counted and bar graphs made to indicate the mouth floral count of each student. The mouth washings were repeated at intervals and the average counts ascertained. The individual counts were then classified according to the number of mouth antiseptic washings per day, and also information was recorded as to whether or not the patient smoked, the number of cigarettes, etc. Direct Breed counts, in which the organisms in the oral and pharyngeal cavities both living and dead were counted and classified, were also made as a check against numerical colony growth. Breed mouth counts varied from 500,000 to 500,000,000 bacteria per cc. of sterile mouth wash water.

GENERAL PROCEDURE.

The immediate effects of the use of different tooth-pastes and U. S. P. mouth washes were evaluated, by preceding the sterile mouth water rinsing with the actual use of tooth-paste or antiseptic mouth wash. Well known tooth-pastes and sterile tooth brushes were used for 1 minute to thoroughly cleanse the teeth. The usual mouth gargling with sterile water for 1 minute was followed with a plating of a fraction or dilution of the resultant gargle water. By comparing the normal flora of each student, and later entire groups of students, with the one made following the tooth brushing, the comparative value of the dentifrice was roughly ascertained. The comparative charts generally indicated a sharp decline in all mouth flora following a thorough tooth brushing, with several well-known commercial tooth-pastes. In the same manner 30 odd U. S. P., N. F. and proprietary mouth washes were evaluated, noting the decrease or increase in the number of mouth bacteria for each student following the use of the various mouth washes. The usual bar graphs were drawn up for comparative purposes. The U. S. P. and N. F. mouth washes were tabulated according to their apparent efficiency in lowering the mouth flora, the proprietaries for obvious reasons were not specifically named on the charts. The time interval between the tooth brushings, or antiseptic mouth washings, and the original sterile water garglings were varied in order to find out how long it took before the bacteria were inhibited or killed by the tooth-pastes and mouth washes used. Statistical tabulations were then attempted based on the apparent time lapse for effective germicidal activity of each medicament. In recent groups of students, a record was kept of colds, influenza and other upper respiratory infections during the school year for comparative and tabulation purposes.

CONCLUSIONS AND INTERPRETATION OF RESULTS.

1. The statistical results generally indicated the value of correct oral hygiene habits in lowering the incidence of the respiratory infections, by decreasing the number of nasal and mouth flora of pathogenic bacteria.

2. The clinical and dental value of frequent tooth brushings with standard antiseptic tooth-pastes and powders was substantiated by noting the comparative counts with the resultant decrease in the number of oral and gingival membrane bacteria.

3. The results suggested a possible comparative table based on direct "*in vivo*" finding for the bactericidal activity of various U. S. P. and N. F. mouth washings using plate and Breed count techniques. Tooth-paste evaluation might be determined by a similar procedure.

4. The oxidizing antiseptic mouth washes. Dakin's Solution, sodium perborate and hydrogen peroxide in 50% solution apparently increased the number of mouth bacteria per cc. during the first half hour. Later the number dropped markedly, suggesting the mechanical action of the oxidizing mouth washes in liberating the bacteria from the intercellular spaces of the buccal membranes, interdental spaces, etc.

5. The results indicated variations in the time interval for the effectiveness of the bactericidal activity of mouth washes, as in many cases the organisms were not destroyed or growth inhibited until one-half to one hour after gargling.

6. Incidentally it was found that immediately after smoking, the mouth flora count appeared to be lowered, although after a time the count took a sharp upward rise, in some cases, even above the normal. Hot tobacco smoke tends to inhibit the growth of mouth bacteria, particularly destroying the highly sensitive thermolabile hemophyllic group of bacteria. However, the smoke dust particles may injure the oral epithelium, thus nullifying any hot smoke or nicotine antiseptic action, by irritating the defense mechanism of the mucous membranes.

7. Repeated microscopic Breed count studies of the mouth flora of 400 odd students revealed only a few spirillæ or protozoan microörganisms, such as the *Treponema refrigens*, *Treponema Vicenti* or *Endamœba Gingivallis*, suggesting that mouth diseases are less apt to occur among the young than among adults, particularly where oral hygiene habits are the rule.

8. Sore throats, particularly among teachers, may be incited by inhalations of chalk dust, which set up mechanical irritations. The sputa of teachers so infected showed chalk dust in several samples.

9. Breed count mouth flora varied from 130,000 to 95,000,000 per cc. of wash water, in an average class of students; the Breed count included both living and dead bacteria.

10. Colony counts without the use of antiseptic mouth washes ran as high as 2,000,000 and as low as 70,000 in an average class of students. The use of tooth-paste caused average drops to as low as 10,000 after thoroughly brushing the teeth with a good dentifrice.

11. Nasal and oral insufflations of 10 per cent argyrol proved effective in acute rhinitis in causing a sharp drop in the bacterial flora.

12. Boulton's solution proved to be the most valuable of the mouth washes tested for all periods from 10 minutes to 1 hour after its use, with colony counts running as low as 3000 per cc. Alkalinus Aromaticus and Dobell's Solution gave mouth counts varying from 8–14,000 colonies per cc.

13. Liquor antisepticus and chloroform water appeared to be more effective half an hour to 1 hour after gargling, with viable mouth counts varying between 10 to 20,000 per cc. rinse water.

14. The three nationally advertised proprietary mouth washes tested showed favorable results at the end of 1 hour, with plate counts giving as low as 3000 for viable bacteria per cc. of rinse water.

15. The germicidal action of mouth washes tended to be transient; while effective tooth-paste and brushing had a more lasting antiseptic action, the mouth flora remaining lowered for several hours.

16. The ratio of the mouth counts was inversely proportional to the number of brushings per day. For whole groups of participating students the lowest mouth counts were obtained from those who habitually brushed their teeth 3 times a day. The next lowest counts came from those who cleansed their teeth twice a day. The highest counts were obtained from the very few students who did not cleanse their teeth at all, and the next highest from those who cleansed their teeth once a day only. These results were the most conclusive obtained in this study over a period of 4 years.

17. Ten per cent solutions of ordinary table salt proved very effective in causing decreased mouth flora in most test cases.

18. Ordinary sterile water used as a mouth wash caused decreased mouth floral counts in some instances, but the results were subject to wide variations in individual instances. Similar results were obtained after eating oranges or lemons.

SUMMARY.

The study supported clinical and dental evidence of the practical bactericidal value of the regular use of tooth-pastes and mouth washes in keeping down the usual mouth flora of pathogenic microörganisms.

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THE FIRST PHARMACIST IN NORTH AMERICA.[1]

BY THEODORE J. BRADLEY.[2]

In City Hall Square of the City of Quebec there stands a monument to the Canadian pioneer, Louis Hébert, who was probably the first pharmacist to establish his home and practice his profession in North America. Undoubtedly there were some pharmacists among those who accompanied Columbus, the Cabots and other explorers who discovered and visited various parts of the Americas, and some pharmacists are known to have visited this continent before Hébert came here; but we have been unable to find any indication of their having become residents. Though the records of Hébert and his work are not complete, enough is known about him to make a story of great interest.

The Atlantic coasts of Canada and New England had been visited by the Norseman, Leif Ericson, in about the year 1000, but the records of this visit are fragmentary and were forgotten for a long time. At the time Columbus discovered America, in 1492, another Genoese in foreign service, Giovanni Cabato, who is better known to us as John Cabot, had been sailing the North Seas in the service of the merchants of Bristol, England, searching for some islands thought to be in the Atlantic Ocean, far west of Ireland. When news of the discoveries by Columbus reached Cabot, he secured authority from King Henry VII and organized an expedition to sail further west than before. On June 24, 1497, he discovered land, which we now call Cape Breton Island, and the smaller St. Pierre-Miquelon Islands. The next year, in 1498, he returned with a larger expedition and explored the coasts of Labrador, Newfoundland, Nova Scotia and New England. John Cabot died soon after his return to England, in the fall of 1498, and one of his sons, Sebastian Cabot, became almost equally famous as an explorer, in the service of various countries.

John Cabot's explorations and discoveries gave England a claim to the northeast coast of North America which ultimately prevailed, but the claim was not asserted at first, and fishermen from France, Spain and Portugal, as well as those from England, were the first to take advantage of the resources of the newly discovered lands and waters. These fishermen frequently visited Newfoundland and the mainland, but no regular settlements were established for some years—in

[1] Section on Historical Pharmacy, A. PH. A., Portland meeting, 1935.
[2] Dean of the Massachusetts College of Pharmacy, Boston.

Newfoundland probably not until about 1578 and more certainly by Sir Humphrey Gilbert in 1583 and John Guy in 1610.

In the meantime, explorers and missionaries were working in this rich field. Jacques Cartier, a Frenchman, discovered the Gulf of St. Lawrence in 1534, and in 1535 he sailed up this river for about a thousand miles, to the Lachine Rapids, near the site of the present city of Montreal. During the next sixty or seventy years, fishing, fur trading and missionary activities continued, and some attempts were made to establish settlements on the mainland, but these were not successful until after the beginning of the next century.

Looking back at these activities from our modern point of view, we may be surprised at the extremely slow rate of settlement of the western hemisphere. Columbus established the present city of Santo Domingo on the island of Hispaniola or Haiti in 1493, the year following his discovery of the Bahamas and that island in 1492. This was followed by the settlement of San Juan, Puerto Rico, in 1508 or 1509. Probably the first settlement on the mainland was at Panama, in 1519, followed by that of Cartagena, Colombia, in 1533; and it was not until 1565 that the first settlement in North America was made, at St. Augustine, Florida. Several other more or less permanent settlements were made on various islands, like those mentioned on Newfoundland, late in the sixteenth century. It was not until after the beginning of the seventeenth century that the tide of settlement flowed strongly, beginning with Port Royal, in Acadia (now Annapolis Royal in Nova Scotia), in 1604, and Santa Fé, New Mexico, in 1605. These were soon followed by Jamestown in Virginia, Quebec, New York and Plymouth.

Port Royal was settled under royal warrant by Pierre de Guast, Sieur de Monts, in 1604, as stated above, after an exploratory voyage in 1603, during which he visited the lower St. Lawrence and nearby lands. This was during the reigns of Elizabeth and James I in England and of Henri IV in France. It was a time of civil wars and religious persecutions, and these conditions contributed a great deal to the unrest which resulted in the establishment of several of the early settlements in America. The party of de Monts included a friend, de Poutrincourt, the subsequently famous Samuel de Champlain, and an apothecary, Louis Hébert.

Very little is known about the early life of Louis Hébert. We have been unable to ascertain the date of his birth. It is recorded that he was a native of Paris and the son of an apothecary, and that he was himself a court apothecary when he became a member of the emigrant party of de Monts.

While he was in Port Royal, Hébert practiced as an apothecary and supplied medical advice and medicines to his fellow Frenchmen and the Indians. During this time, there was a severe outbreak of scurvy in which his services were helpful. Among the Indians to whom he gave medical service was the prominent chief, Membertou. Hébert was a devoted lover of the soil, and in Nova Scotia he began the work in agriculture which he pursued along with his practice of pharmacy during the remainder of his life. This work in agriculture made him the first Canadian farmer as well as the first pharmacist.

England claimed Acadia and other nearby lands, and in 1613 the small settlement of Port Royal was attacked and nearly destroyed by English from Virginia, who held the town for several years. In 1614, Hébert and most of the French resi-

dents returned to France. The province of Acadia, including the settlement of Port Royal, was passed back and forth between France and England several times, but ultimately came under the control of England, and the names were changed to Annapolis Royal for the settlement and Nova Scotia for the province.

Samuel de Champlain did not remain with the de Monts party for long and soon began the series of explorations which made him preëminent among Canadian pioneers. In 1608, he established a settlement on the site of an Indian village, Stadaco, which came to be called Quebec, and in 1617 he induced his old friend and companion, Louis Hébert, to try his fortune again in Canada. In the French National Library there is preserved a letter from de Monts, dated February 18, 1617, which discusses the possibilities of the development of Canadian resources and is highly complimentary to Hébert. Many difficulties had to be overcome before Hébert was able to leave France, and the ship in which he and his family sailed had a very stormy passage lasting thirteen weeks. At times all hope of reaching their destination seemed lost, but they finally sailed up the St. Lawrence and landed at Quebec, and Hébert's life there during the next ten years was one of fruitful achievement. The records indicate that he was immediately recognized as a leading citizen. Soon after landing he received a grant of land, which he worked along with his practice of pharmacy. He was indefatigable in his efforts to develop the resources of the country, and was given the title of Royal Procurator. In 1626 he received a grant of the Fief of St. Joseph in the outskirts of Quebec, and the title of Sieur D'Espinay was conferred upon him, in recognition of the fact that his was the first French family to establish itself in the country.

Hébert Monument in the city of Quebec.

The career of Hébert was cut short in January 1627, when he died suddenly as a result of injuries received in a fall, leaving a widow and three children. He was buried in the cemetery of the Récollet fathers. Fifty years later his body was disinterred and placed in the vault of the then new convent of the Récollets in the upper town of Quebec.

Madame Hébert, born Marie Rollet, was a remarkable woman who lived for many years after the death of her husband. When Quebec was first captured by the English, in 1629, two years after the death of Louis Hébert, and many of the French inhabitants went back to France, Madame Hébert decided to keep her family in the colony, and it is recorded that this was one of only two permanently estab-

lished families remaining in Quebec. When the colony was restored to France, in 1632, a Mass of thanksgiving was celebrated in the home of Madame Hébert.

Louis Hébert's older daughter, Anne, married Étienne Jonquest, a Norman colonist in 1617, and it is believed that this was the first Christian marriage in New France. In 1621, the younger daughter, Marie, married Guillaume Couilliard de Lespinay. Many Canadians trace their descent from Louis Hébert, through these daughters and his son, Guillaume Hébert.

Many pharmacists have distinguished themselves in other lines of work than pharmacy, but Louis Hébert is perhaps the only one of these who won renown as a pioneer, and it was because of his work in developing the resources of Canada that the monument to him was erected in Quebec City Hall Square in 1918. His work as the first pharmacist to settle in North America is commemorated by a tablet in the town hall of Annapolis Royal, Nova Scotia, erected by the Nova Scotia Pharmaceutical Association and unveiled by the Canadian Pharmaceutical Association on August 2, 1930, with very impressive exercises, which were attended by the writer of this article as the delegate representing the AMERICAN PHARMACEUTICAL ASSOCIATION. The exercises included an address by the Reverend Abbé A. Couilliard-Despres, a direct descendant of Louis Hébert, through his younger daughter.

His background and early training did not prepare Louis Hébert very well for the rough life of a pioneer. Most of the colonists who came to New France during the first years of the seventeenth century were Norman peasants, prepared for the hardships of pioneers by their arduous work on the farms of Normandy. Hébert was a Parisian and an apothecary, with none of these advantages. It is unfortunate that there was no contemporary biographer to record his varied and helpful achievements in developing the resources of Canada. His history is closely intertwined with that of the settlement of the colony, and is found in the fragmentary references to him in the records of the settlement of Port Royal and Quebec. Hébert accomplished a great deal by quiet persistent work, without romantic appeal, and he was not a popular hero like Cartier, Champlain or Frontenac, but he is preëminent among those who followed the explorers of Canada and worked successfully to develop and maintain their settlements in the New World.

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"The characteristic of American history is that everything appears to happen by accident. Nothing seems planned or intended. Other nations adopt policies and pursue them; their history is formed by the clash of these policies. But America moves by a kind of indirection. Always in American history the unintended, the apparently irrational, happens." "Credo," condensed from the *Saturday Evening Post* by *Readers Digest* for May.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

"More and more educational institutions are establishing their own radio stations and are sending out programs of instruction to the people of their states. Through Station W-B-A-A, on the Campus of Purdue University, the people of Indiana have been informed regarding events of importance occurring on the campus, information on general subjects and information on specific subjects. Fortunately for the School of Pharmacy, fifteen minutes are set aside every week for the use of the staff. This period has become known as "The Apothecary Hour" and each week some member of the staff presents topics that are thought to be interesting to the citizens of the State. The following two radio talks by Professors Lee and Klemme indicate the type of thing that is being done.—C. B. JORDAN, *Editor*.

FALLACIOUS ADVERTISING.

BY C. J. KLEMME.

No matter where we go, nor what we do, as long as we are in contact with civilization we meet the blessing and curse of organized business, *viz.*, advertising. We are aroused from pleasant thought after listening to a beautiful program on the radio only to hear some zealous radio announcer dinning into our ears the marvelous qualities and virtues of some tooth-paste, mouth wash, gasoline, baby food, effervescent salt, cold remedy, body-building breakfast food, soap, dog food or other article of commerce without the use of which in the immediate future, we will surely suffer unspeakably from decayed teeth, halitosis, a stalled automobile, an undernourished baby, chronic constipation, pneumonia, weak bodies, dull gray clothes or a blemished skin, or the possession of a mangy pup. We see the same things in print, staring at us from the pages of our newspapers or favorite magazines. In the street cars, on the bill boards, on placards and posters we encounter in an endless stream the announcements of things for sale together with the usual ballyhoo. To see and hear these things, many of them as fantastic as the Tales of Baron Munchausen, is as inevitable as eating and sleeping, as unavoidable as death and taxes.

Yet, advertising is absolutely necessary to our economic existence. Without it, the commerce of the world would dwindle to the vanishing point. It is the very breath and pulse of any far-flung business enterprise. If it were not for this constant emanation of facts and fancy which we call advertising, how would John Doe of Podunk know that Richard Roe, Inc., of New York, manufactured in quantity the very article he needs, and how could Richard Roe, Inc., dispose of, at a profit, the products of quantity manufacturing without broadcasting to the world that such and such articles are available?

It is not with genuinely honest advertising that I have any desire to pick a bone, but the fallacious advertising, the misleading, erroneous, deceitful and downright false statements made about articles, some of which are no better than dozens of others of similar kind, some of which are not worth carrying home, and some of which are actually dangerous or detrimental. Those people in professions concerned with the public health, *viz.*, medicine, dentistry, pharmacy, etc., probably notice and resent this type of advertising more than anyone else, largely because so many

products for internal use are often misrepresented. And yet there are many other kinds of products offered to the American public along with statements that should make even the most gullible person turn a deaf ear to them. When we see and hear about the fine qualities that can be found in one and only one brand of gasoline, and the advertiser writes or speaks with such force and fervor that one would think he actually believed these things himself, we wonder why, if we use another brand of gasoline, our car *ever* started, not to mention a cold morning. There are good gasolines and good oils, but don't expect a five-year old automobile engine to perform miracles under their influences. That smacks too much of rejuvenation, but the advertisers would have you believe their products will do just such things for our old 1928 Senile Sixes.

The vitamins, so mysterious, so intriguing, so popular, come in for more than their share of abuse. To be sure, these substances are necessary for the normal functioning of life processes, and sadly enough many diets and many foods are lacking in these important food accessories. The general public has been made aware of these facts largely by fanciful items in the tabloids and in the advertisements of certain foods and pharmaceutical products. The chief trouble with such advertisements is that so many of them are extreme exaggerations and the advertisers would have us believe that if we failed to use their own particularly vitamin-rich product, our diets would be seriously impoverished and we would suffer accordingly. On the other hand, some of the powers attributed to various products by virtue of their vitamin content are truly amazing. Colds may be cured magically, pounds and pounds of weight may be added to the body, all sorts of ills and ailments may be prevented and many other startling miracles are alleged to happen under the influence of these vitamin products. Yet there is much truth contained somewhere in these wild claims, so much in fact that we cannot always say that a given claim is actually false. It is simply a fallacious claim; perhaps we may say it is the truth, twisted, stretched and distorted beyond recognition. We have a pronounced example of this in the statement that certain antiseptics have unusual germicidal powers. It may be true that a given antiseptic will kill germs in ten seconds. Undoubtedly, that is a very true statement. But what the advertiser fails completely to mention is the kind of germs which are executed so suddenly, and the conditions under which said execution is carried out. As a matter of fact the poor germs haven't a chance. Let us consider an analogy. The rays of the sun are healthful, beneficial and energy giving. Yet they can be as deadly to us as any machine-gun, perhaps not as *rapidly* fatal as the gun, but none the less sure. A person who might be exposed directly to the sun's rays for a few hours would become so severely sunburned that he could not survive. In our ordinary, every-day life we are protected from this deadly action of sunshine by clothes, trees, buildings and other things. So it is in what we might call the ordinary, every-day life of a germ. Bacteria, like ourselves, are not in the habit of exposing themselves unduly, and they find their best living conditions in the microscopic crevices and abrasions of the tissues where they are snug and safe from the terrors of their "Aunty Septic." On the other hand, if we put these bacteria in a test-tube and subject them to the direct action of the antiseptic to be tested, it is no wonder they curl up and die in ten seconds. The test-tube becomes their execution chamber in which they have no protection, but let the same antiseptic be used on the tissues,

for example in the mouth, and immediately after its use a bacteriologist could demonstrate the very real and actual presence of bacteria, as full of life and kicking as strongly as ever. Thus we find that the behavior of an antiseptic is far different when applied to tissues than when it is turned loose on some poor, helpless bacteria in a test-tube, and when an advertiser claims that his antiseptic will kill germs in ten seconds, he is telling you the unsullied truth, oh quite the truth, but as the Queen of Sheba said: "The half has never yet been told!"

For the past six or seven years the public has been made hyperconscious of the dangers of acidity and the benefits of alkalinity. Like the abuse of the vitamins, there are truths in what is said about acidity and alkalinity but some of them are carried too far.

It is true that the blood and tissues of the body have a definite alkalinity and this alkalinity must be maintained within very narrow limits in order for life to exist. We have in the body what is known as the alkali reserve, and, if this reserve is well built up, the body is more resistant to common infections. This fact has been the basis for a great deal of advertising on alkalinity and many products are claimed to increase the alkalinity of the body. Actually, many of them do nothing of the kind. One ailment we hear and read so much about in various advertisements is the acidity of the stomach. This or that product is recommended to be taken in the case of hyperacidity of the stomach. Curiously enough, we may have a condition which appears very much like hyperacidity but is actually due to a lack of the normal amount of acid that should be present in the stomach. Under this condition rapid fermentation takes place, producing organic acids which give this sensation of hyperacidity. In such instances the use of alkaline salts to combat the acidity is probably the worst thing that could be done. One should not continually use such alkaline salts to combat stomach disorders over a long period of time unless it be on the advice of competent medical authority, because the condition may be a serious, chronic disorder which demands medical attention.

In a way one cannot criticize manufacturers for employing these extreme measures to convince the public that their products are the best on the market, especially when their products have keen competition. Nevertheless, one should use common sense and exercise perhaps a good deal of skepticism when he reads or hears some of the claims that are made.

Thus far the advertising which we have considered is for the most part quite harmless and, while most of the statements may be true, they are merely distorted truths and very little in the way of actually false statements may be found. The truly vicious and deceitful type of advertising is largely found in connection with what we might call "cure-all" medicines. These are generally patent medicines or those of which the manufacturer keeps the formula a profound secret. Usually we find such remedies advertised as being sure cures for headaches, stomach trouble, liver disorders and all kinds of complaints. As a general rule, we might say that the greater the claims for these remedies, the more they should be avoided.

The question naturally arises as to how one may separate the wheat from the chaff in the advertisements that we see and hear. If you are in doubt as to the validity of an advertising statement, consult some one who is an expert in the field of the product about which you are interested. If the product is sold in a drug store, consult your local druggist, and I am sure that he will give you the most

honest information that is available about the product concerned. When it is a question as to the use of some medicine or various remedies, consult your physician. He is a highly trained specialist in this field and his advice is the best that you can obtain.

PHARMACY THROUGH THE AGES.

BY C. O. LEE.

HERBALISTS AND THEIR HERBS.

Modern medical practice is much less dependent upon crude drugs and their preparations than that of generations past. It is interesting to note, however, the importance of vegetable and animal drugs in ancient materia medica. This is a story about ancient herbalists and their medicines.

HERB DOCTORS IN OUR DAY.

During the first decade of the present century I served my druggist's apprenticeship in a drug store in a small town in southeast Kansas. In the town there lived an old Indian Herb Doctor. At least he was known as a doctor, and claimed to be part Indian and to know something about Indian herbs and medicines.

He used to spend a day, now and then, in the woods gathering herbs. These he used, presumably, in preparing his famous tonic which he sold in the mining towns of that region.

The old doctor came to our drug store and made small purchases of a few things which could not be found in the woods. He was an interesting character. His hair was long enough to fall leisurely about his stooped shoulders from beneath a broad brimmed hat. He was not much of a conversationalist but was interesting when he talked. His remarks were often critical and pessimistic, yet he was, on the whole, rather philosophical.

He had a shed for a laboratory and a medicine wagon, properly decorated, for his sales excursions. The old doctor was not well known to his neighbors; he revealed no medical secrets and minded his own business.

This story is not, I am sure, an unusual one but it is an example of the secrecy and mystery which so often surrounds makers and sellers of strange medicines. It shows, I think, that certain herbal systems appeal to those anxious folks who never cease to be concerned about their ailments, whether real or imaginary. It has always been so and will continue to be for many generations yet to come.

FAITH IN HERBS.

We will never know who were the first to use plants and herbs as medicines. Neither are we sure that herbs were first used for purposes of curing diseases or whether they were used to discourage evil spirits or demons presumably responsible for the afflictions of mankind. At any rate plants have been used by all primitive peoples, so far as we know, for healing the sick and for purposes of poisoning enemies. Many plants are poisonous when taken in amounts larger than medicinal doses.

The savage learned all of this by many sad experiences, no doubt, and made

use of the knowledge he had gained whenever he could. Primitive peoples, not unlike ourselves, feared disease. In their attempts to cure or frighten away disease it is quite possible that their patients succumbed to the treatment rather than the ailment. We sometimes feel that this happens to us even to-day.

PLANT LORE AND SUPERSTITION.

Plant lore of primitive folks was not free from their superstitions. The appearance of the parts of plants used, the conditions under which they had grown, were gathered and prepared for use, were often of great significance. For example, three rather well-known root drugs, because of their forked, human-like shape were, according to tradition, possessed of strange properties. One of them, Mandragora, was used by the Greeks in their love potions. Mandrake is mentioned in the old testament as an antisterility cure. Ginseng, which at one time grew abundantly in the woods of Indiana, is highly prized by the Chinese and Koreans as a panacea for all ills; so far as we know, it is practically inert. The more nearly like the human form the Ginseng roots are the more valuable they become.

It is interesting that fetishism for certain crude drugs has continued through thousands of years of human history. The reputation that such and such a medicine is a very old secret remedy appeals to the daily run of imaginations, while the facts of science go unheeded.

ANCIENT HERBAL DOCTORS.

The nations of antiquity, it seems, had their herbalists who knew something about plants and their uses in the treatment of disease. Among these peoples may be included the Sumerians, Egyptians, Indians, Chinese, Babylonians, Persians, Assyrians, Nubians and, perhaps, others. The primitives of all of these peoples associated the curative properties of plants with their gods. As the priesthood developed the priests were often the ones who knew plants and their uses. The priests, it was assumed, got their information from the gods whom they served and worshiped.

In their ministrations the priests learned the value of suggestion and mixed psychology with their medical treatments. The patients, in addition to swallowing bitter decoctions, had to listen to the songs and incantations of the ancient crooners. Even so the minds of the patients were diverted from their own miserable selves and centered upon the utterances of the soothsayers. Under such conditions medicines were doubtless less bitter and pains less severe.

Coleridge was surely right when he said, "The best inspirer of hope is the best physician."

CHINESE AND INDIAN HERBALS.

The Chinese system of medicine and pharmacy has existed hundreds of years with but slight change. Many strange philosophical explanations and beliefs have been woven into their knowledge of anatomy, physiology and pharmacology. Their materia medica comes largely from the plant and animal kingdoms, although they use a number of inorganic minerals and their compounds. The old system is giving away slowly to modern medical science.

Early Indian herbal medical practices are rather obscure although they must have existed.

EGYPTIAN GODS AND GODDESSES OF MEDICINE.

Primitive peoples everywhere, it seems, associated the art of healing with their gods and considered it a divine art. These people lived in the great out-of-doors and depended for a living upon the plants that grew about them, whether wild or cultivated. Their gods were gods of the natural world who knew all about vegetation, the heavens and plants of medicinal virtue.

Osiris was such a god to the Egyptians. The wonderful *Maat* plant was in the form of the body of Osiris. His followers ate the plant and, in so doing, became like the god they worshiped and lived on forever. A beautiful idea for childlike imaginations.

Isis, the twin sister, wife and protector of Osiris was a great herbalist and magician. She used her magical powers perhaps more than her skill as an herbalist, although according to tradition she made good use of both.

SCHOOLS OF HERBALISTS.

It is thought that schools of herbalists existed in Egypt as early as 3000 B. C. The works of such schools have not, however, come down to us.

It has been stated that magic played such a prominent part in early medical practices that it is difficult to find an account of herbal science free from the feats of magic. Budge says that, "the progress of herbal science was strangled by the belief in magic which was general among the people."

ASSYRIAN AND SUMERIAN HERBALS.

From the sources of information at hand it would seem that the Sumerians and early Egyptians were contemporaries and perhaps gained much of their early medical and herbal knowledge from a common source. Sumerian herbals are said to have existed in the third millenium B. C. A Sumerian tablet, in the British Museum, has a note attached which states that it was copied from a tablet written about 2200 B. C. Copies of other medicinal texts have also been found which are much older than the one just mentioned.

Some knowledge of Assyrian Herbals has been obtained from the fragments of the clay tablets which have been found among the ruins at Nineveh. Thompson, in 1924, prepared a monograph entitled *Assyrian Herbal*. As a result of Thompson's studies it is known that the Assyrians knew about 250 vegetable drugs and about 120 mineral drugs in addition to many others which, as yet, remain unidentified.

The Assyrian herbalists arranged their drugs according to their needs. It is quite obvious that the doctors and chemists of Nineveh knew a great deal about their herbs and their uses. They established "physic gardens" as a means of assuring themselves constant and reliable sources of useful medicinals. These gardens were often founded in connection with the temples and palaces. This fact indicates a considerable advancement in the matter of protecting the source and quality of their drug plants.

In Assyria, as in other ancient countries, the herbalist physician did not resort to the use of drugs alone in the treatment of the sick. He worked with the priest and the seer. The patient had to endure three doctors in one treatment. The physician prescribed the herbs, the priest recited songs and prayers and the seer interpreted the signs and omens which were in evidence. Even so three doctors

should be better than one any time, especially if each were a specialist in his own field, otherwise they might not agree.

GREEK HERBALS AND HERBALISTS.

Like the Egyptians, Sumerians and Assyrians, the Greeks believed that the gods were the first herbalists and physicians.

The Greek Herbals were compiled by the lay herb-doctors and physicians who were known as the Asclepiadæ. They wandered about the country and made their living by treating the sick wherever they found them.

Hippocrates (B. C. 460–377) is known as the "Father of Medicine." He is supposed to have learned a great deal about medicine from the Egyptians and to have been the founder of a scientific system of medicine. He tried to clean things up by banishing superstition and magic from the practice of medicine. He used about 400 drugs in his practice, most of which were vegetable in character. So far as is known he compiled no herbal but undoubtedly made use of those known.

The first Greek Herbal was compiled by Diocles Carystius in the fourth century B. C. This Herbal is not extant to-day, but was a list of plants, their habitats and their medicinal properties.

Aristotle (B. C. 384–322) is credited with *De Plantis*, a list of over 500 plants, which is included in his numerous works.

Theophrastus (B. C. 372–285) in his *Historia plantarum* described over 500 plants. He is referred to as the first scientific botanist rather than a medical botanist.

Herophilus, in the third century B. C., made up heterogeneous mixtures of vegetable drugs and gave them in large doses to his patients. He was criticized for his large doses.

Crateuas (B. C. 120–63) was a great herbalist and in his Herbal he made drawings for the plants he had named.

Perhaps the greatest of the ancient herbalists was Dioscorides who lived in the first century A. D. He was, for a time, physician to the Roman army in Asia. He also traveled extensively in Europe and got his information about plants first-hand. He is famous for his work of five books known as De Materia Medica.

He compiled information which had been made available by the herbalists who had preceded him. To this he added the information which he gained by experience and travel. His Herbal was so complete and well done that our modern Pharmacopœias still contain many of the drugs which he described and used.

Other famous herbalists could be named but we must close with a brief mention of Galen who lived A. D. 130–200. Budge says, "The Greek Herbal assumed its final form in the hands of Claudius Galen,——." He traveled extensively and is credited with having written about 400 works; 275 of these were of a medical nature and 83 of them are extant and considered genuine. His entire works have never been translated. Galen was famous, among other things, as a medical teacher. His Herbal, *De Simplicibus*, was contained in Books VI, VII and VIII of his chief work. It was so nearly final that it was never superseded by succeeding Greek and Roman botanists.

The head of this famous physician and pharmacist may be seen as the keystone in the arch over the front entrance to the pharmacy building on our campus.

(*Scientific Section Continued from Page 618.*)

A CHEMICAL STUDY OF THE FIXED OIL OF POKE ROOT.*,[1]

BY SAMUEL W. GOLDSTEIN[2] AND GLENN L. JENKINS.

The root of *Phytolacca americana* (*decandra*) Linné (poke) has been an official drug since 1820 but no report has been published on the constituents of the fatty oil which this root contains. The present work was undertaken in the course of a complete phytochemical study of poke root.

The root used in this work was supplied by S. B. Penick and Sons and was collected near Asheville, North Carolina.

EXPERIMENTAL.

Twenty-two kilograms of finely powdered poke root were extracted with petroleum benzin (b. p. 30° to 60° C.) in a Lloyd extractor until the drug was exhausted. Most of the benzin was removed by distillation under reduced pressure, and a current of air was passed over the residue to remove the remaining solvent. The residue was dissolved in hot alcohol and the mixture, on standing over night, formed a deposit and a clear supernatant liquid which was removed.

Isolation of a sterol-like Compound, $C_{22}H_{40}O$.—Small portions of the solid substance gave color reactions with the Liebermann-Burchard (1) and Hager-Salkowski (2) reagents for sterols. In the latter case, however, the red color produced was more pronounced in the sulphuric acid layer than in the chloroform layer. A chloroformic solution of the substance decolorized a bromine solution. The substance was readily soluble in hot ethyl acetate and hot ethyl alcohol, and was deposited from the solutions while still warm, but the coloring matter present behaved in a similar manner. A solution of the substance in hot ethyl acetate was prepared and was boiled with animal charcoal for several minutes, then filtered, while hot, through a Gooch funnel by means of a hydraulic suction pump. On cooling, crystals formed in rosettes. These crystals were removed by filtration and washed with ethyl acetate, then they were dried in an oven for thirty minutes at 95° C. The dried crystals melted at 107–108° C. Tests for nitrogen and sulphur gave negative results.

0.003964 Gm. gave 0.012062 Gm. CO_2 and 0.004326 Gm. H_2O
C = 82.99; H = 12.21 per cent
$C_{22}H_{40}O$ requires C = 83.05; H = 12.13 per cent
0.0280 Gm. dissolved in 14 cc. of chloroform gave $\alpha_D^{26°} = +0.14°$ in a 100-mm. tube.
$[\alpha]_D^{26°} = +70.0°$.

Two portions of the substance were refluxed for two hours with acetic anhydride and acetyl chloride, respectively. The crystals obtained on cooling in both cases were separated and recrystallized. The melting points of 107–108° C. indicated that no reaction had occurred and this was confirmed by running mixed melting points of the original substance with the products obtained by the above treatment. The oxygen present in the molecule apparently is not present in the form of a free hydroxyl group.

The alcoholic solution obtained from the petroleum benzin extractive was freed from alcohol by evaporation and the final traces of the solvent were removed by heating the residual oil on a boiling water-bath under reduced pressure. The oil obtained weighed 96.41 Gm., representing 0.44 per cent of the dried root used. The following constants for the oil were determined: Specific gravity $_{25°}^{25°}$ 0.9209; optical rotation $[\alpha]_D^{26°} = +13°$; refractive index $N_D^{26°} = 1.4741$; acid number 71.97; saponification number 139.43; ester number 67.46; iodine number 69.14.

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* Scientific Section, A.PH.A., Portland meeting, 1935.

[1] From the Department of Pharmaceutical Chemistry, University of Maryland, School of Pharmacy.

[2] Abstracted in part from a thesis submitted by Samuel W. Goldstein to the Graduate School of the University of Maryland in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

Isolation of Free Fatty Acids.—Fifty-five grams of the oil were dissolved in 1200 cc. of ether and the solution was successively extracted with portions of 5 per cent solutions of ammonium carbonate, sodium carbonate and potassium hydroxide.

The ammonium carbonate shakings were acidified with diluted hydrochloric acid, and the mixture was extracted with ether. The ethereal solution was dried with anhydrous sodium sulphate and then the ether was removed by distillation. The oily residue was dissolved in alcohol and the silver salt was prepared using silver nitrate solution. The silver salt was analyzed.

0.474 Gm. of salt gave on ignition 0.0201 Gm. of Ag
Ag = 42.4 per cent
$C_8H_{15}O_2Ag$ requires Ag = 43.0 per cent.

Although the figures thus obtained are in fairly close agreement with those required for the silver salt of an octanoic acid, it is probable that the oily acid substance was a mixture.

The sodium carbonate shakings were obtained in two portions and these were examined separately.

Portion I. The reddish brown aqueous solution was treated with animal charcoal, and, after cooling, was acidified with diluted sulphuric acid and extracted with ether. The ethereal solution was dried and the ether was removed by distillation. The orange-colored residue was dissolved in alcohol and the alcoholic solution was kept at 10° C. The crystals which were deposited in the alcoholic solution were separated by filtering through a Gooch funnel with suction. The crystalline solid (1.75 Gm.) was dissolved in alcohol and recrystallized. After drying in a desiccator, the melting point was 72–73° C. Recrystallization from methyl alcohol and then from glacial acetic acid raised the melting point to 76–77° C. The silver salt was prepared and analyzed.

0.0265 Gm. of salt gave on ignition 0.0063 Gm. of Ag
Ag = 23.77 per cent
$C_{20}H_{39}O_2Ag$ requires Ag = 25.67 per cent.

The above-described substance was thus identified as arachidic acid.

The alcoholic mother-liquor from which the arachidic acid had been obtained was concentrated and kept at 5° C. over night. A small amount (0.55 Gm.) of crystalline matter was deposited and this was removed and recrystallized from alcohol. The crystals melted at 61° C. The silver salt was prepared and analyzed.

0.1229 Gm. of salt gave on ignition 0.0361 Gm. of Ag
Ag = 29.37 per cent
$C_{16}H_{31}O_2Ag$ requires Ag = 29.7 per cent.

The crystals were thus identified as palmitic acid.

The alcoholic mother-liquor from which the palmitic acid had been obtained was further concentrated and kept at 10° C. A solid separated in small spherical bundles of crystals. The solid (0.4 Gm.) was removed and recrystallized from alcohol. The crystals melted at 51° C. The silver salt was prepared and analyzed.

0.1371 Gm. of salt gave on ignition 0.0405 Gm. of Ag
Ag = 29.54 per cent
$C_{14}H_{27}O_2Ag$ requires Ag = 30.72 per cent.

The crystals were thus identified as oxymyristic acid.

The alcoholic mother-liquor from which the oxymyristic acid had been obtained was kept at 5° C., when crystals were deposited. The crystals (0.5 Gm.) were removed and, after recrystallization from alcohol, melted at 59–60° C. The silver salt was prepared and analyzed.

0.0632 Gm. of salt gave on ignition 0.0183 Gm. of Ag
Ag = 28.95 per cent
$C_{17}H_{33}O_2Ag$ requires Ag = 28.6 per cent.

The crystals were thus identified as margaric acid.

Two more fractions (0.5 Gm. and 0.8 Gm.) of crystalline matter were obtained from the alcoholic mother-liquor, and, although the melting points of the crystals were 53–56° and 46–48° C., respectively, the analyses of the silver salts corresponded fairly well with the required results of margaric acid. Apparently some other substance had been removed along with the margaric acid to cause a lowering of the melting point.

The residual alcoholic mother-liquor decolorized a chloroformic solution of iodine. The alcohol was removed and the liquid residue was kept for a short time at 10° C., when it solidified. A silver salt was prepared and analyzed.

0.1115 Gm. of salt gave on ignition 0.0279 Gm. of Ag
Ag = 25.02 per cent
$C_{15}H_{33}O_2Ag$ requires Ag = 27.72 per cent.

The above-described residue probably consisted of oleic acid and some saturated acid or acids which had not been removed by fractionation.

Portion II. The second portion of the sodium carbonate shakings was treated as under Portion I, and the alcoholic solution obtained was kept at 10° C. The crystals (0.5 Gm.) which were deposited were separated by filtration, and, after recrystallization from glacial acetic acid, they melted at 72–73° C. The silver salt was prepared and analyzed.

0.0155 Gm. of salt gave on ignition 0.0037 Gm. of Ag
Ag = 23.87 per cent
$C_{20}H_{39}O_2Ag$ requires Ag = 25.67 per cent.

The crystals were thus identified as arachidic acid.

The alcoholic mother-liquor was concentrated and kept at 10° C. The crystals (1.1 Gm.) which were deposited were removed, and, after recrystallization from glacial acetic acid, melted at 58.5° C. The silver salt was prepared and analyzed.

0.0810 Gm. of the salt gave on ignition 0.0239 Gm. of Ag
Ag = 29.5 per cent
$C_{16}H_{31}O_2Ag$ requires Ag = 29.7 per cent.

The crystals were thus identified as palmitic acid.

The potassium hydroxide shakings from the ethereal solution of the oil had a red color which changed to yellow on acidification with diluted sulphuric acid. The amount of the substance liberated by the sulphuric acid was too small to investigate.

Saponification of Oil.—The ethereal solution of the oil which had been shaken with the alkalis was washed free of alkali by shaking with water, then dried with anhydrous sodium sulphate, and the ether was removed. The oily residue (33.2 Gm.) was very limpid as compared to the original oil. The oil was saponified according to A. Boemer's method (3). After saponification and addition of 200 cc. of water, the liquid was allowed to cool to room temperature and then was extracted repeatedly with ether. The ethereal extractions were thoroughly washed with water and the ether was removed, leaving a reddish brown solid. The residue was dissolved in hot 98 per cent alcohol, leaving a very small amount of an amber-colored oily substance which did not dissolve.

The substance which did not dissolve in hot alcohol was soluble in hot acetone and cold chloroform. It gave negative Hager-Salkowski and Liebermann-Burchard tests for sterols. The substance may possibly have been a hydrocarbon of low molecular weight.

Isolation of Hentriacontane.—The hot alcohol-soluble portion (300 cc. of solution) of the residue obtained from the ethereal shakings, when allowed to cool and stand over night, deposited a small amount of solid matter. The solid (0.5 Gm.) was separated and, after recrystallization from ethyl acetate, melted at 67.4° C. Using an ethyl acetate solution of the substance, faintly positive tests for sterol were observed. The crystals were not affected by concentrated sulphuric acid, and they did not react with acetic anhydride. After recrystallization from chloroform and then from alcohol, the melting point was found to remain at 67.4° C.

The above-described substance, from its manner of isolation, chemical inactivity and melting point, was identified as hentriacontane.

Isolation of a Sterol (Phytolaccasterol) $C_{30}H_{50}O.H_2O$.—The alcoholic solution from which the hentriacontane had been obtained was concentrated to one-half its volume (150 cc.) and allowed to stand. Crystals, in the form of platelets, formed in a few hours. The crystals (1.0 Gm.) were removed and recrystallized from a mixture of ethyl acetate and alcohol (1:1), and then from ether. The melting point was 168–169° C. Further recrystallization from ether raised the melting point to 169–170° C. A chloroformic solution of the substance decolorized a bromine solution. Color reactions were observed with the Liebermann-Burchard and Hager-Salkowski reagents for sterols, but in the latter case the sulphuric acid layer exhibited a deeper red than the chloroform layer.

0.004191 Gm. gave 0.012413 Gm. CO_2 and 0.004467 Gm. H_2O
C = 80.78; H = 11.93 per cent
$C_{30}H_{52}O_2$ requires C = 81.00; H = 11.79 per cent
0.0710 Gm. after heating for 4 hours at 106° C. lost 0.0029 Gm. of H_2O. H_2O = 4.08 per cent
1 molecule of H_2O of hydration = 4.05 per cent
$C_{30}H_{52}O_2 = C_{30}H_{50}O.H_2O$
0.0303 Gm. dissolved in 15 cc. of chloroform gave $\alpha_D^{26°} = +0.07°$ in a 100-mm. tube
$[\alpha]_D^{26°} = +35.0°$.

The compound was boiled with acetic anhydride for 3 hours. On cooling, platelets with a mother of pearl lustre were formed. The crystals were separated from the solution by filtration and after recrystallization from alcohol and then from ether the melting point remained at 183–183.5° C. The acetyl derivative was recrystallized again from petroleum benzin and only perfectly clear platelets were used to determine the melting point which was 183–183.5° C.

0.0518 Gm. reacted with 1.13 cc. of 0.1*N* KOH
Gram molecular weight = 458.4 Gm.
0.004008 Gm. gave 0.012039 Gm. CO_2 and 0.004326 Gm. H_2O
C = 81.92; H = 11.33 per cent
$C_{32}H_{52}O_2$ requires C = 81.97; H = 11.19 per cent
Gram molecular weight = 468.4 Gm.

The original compound recovered from the saponification mixture and recrystallized from alcohol melted at 169–170° C.

The compound $C_{30}H_{50}O$ described above was proved to be a monohydroxy sterol isomeric with the amyrins (m. p. 170° C.) isolated by Tschirch and Cremer (4) from the different sorts of elemi. Vesterberg (5) resolved the amyrins into alpha-amyrin (m. p. 181–181.5° C.) and beta-amyrin (m. p. 193–194° C.). He also prepared the acetyl derivative of the unresolved amyrin and found it to melt at 200° C., and on crystallizing from ligroin solution obtained two crystalline forms, *i. e.*, leaflets and prisms, which he identified as alpha-amyryl acetate (m. p. 220° C.) and beta-amyryl acetate (m. p. 235° C.). Attempts to resolve the acetate of the compound isolated by us into more than one compound were unsuccessful, and the different melting point obtained with clear leaflets from benzin solution indicates that the compound differs from the previously reported isomers.

The mother-liquor from which the sterol had been obtained, on further concentration and standing, yielded another small crop (0.1 Gm.) of the same compound.

Isolation of Combined Fatty Acids.—The alkaline, aqueous solution which had been extracted with ether was acidified with diluted sulphuric acid. The solution was found to contain formic acid by testing with ammoniacal silver nitrate solution. The solution was then extracted repeatedly with ether. The aqueous solution remaining after the ether extractions was neutralized and evaporated to dryness on a water bath. The residue, after extraction with alcohol-ether and removal of the solvent, gave a faintly positive test for the presence of glycerin. The ethereal solution of the liberated fatty acids was dried and the solvent was removed. The residue, on cooling, solidified to a dark reddish brown mass. The solid (1.0 Gm.) that separated was removed, and after recrystallization from alcohol, ethyl acetate and finally from a mixture of ethyl acetate and alcohol, the granular product melted at 75–76° C. The silver salt was prepared and analyzed.

0.0652 Gm. of salt gave on ignition 0.0169 Gm. of Ag
Ag = 25.6 per cent
$C_{20}H_{39}O_2Ag$ requires Ag = 25.67 per cent.

The substance was thus identified as arachidic acid.

The mother-liquor was concentrated and kept at 10° C. The solid (0.5 Gm.) which separated was removed by filtration. The solid appeared to have adsorbed some amber-colored oily substance which caused part of the mixture to liquefy when the mixture was heated to about 27° C. The solid was dissolved in alcohol and precipitated as the colorless silver salt, which was analyzed. The colored portion remained in the alcohol.

0.0614 Gm. of salt gave on ignition 0.0173 Gm. of Ag
Ag = 28.17 per cent
$C_{17}H_{33}O_2Ag$ requires Ag = 28.6 per cent.

The substance was very probably margaric acid with some impurity which appeared to be some of the original oil that had not been saponified.

The mother-liquor was again concentrated, and, when no solid separated on cooling, the remainder of the solvent was removed. A mixture of solid particles in oil was obtained. An attempt to separate the oil from the acids by forming the sodium salts of the free acids and removing the oil by extracting with ethereal solvents was unsuccessful. The acids were again liberated with diluted sulphuric acid and the mixture was extracted with chloroform. The chloroform was removed, leaving 13.5 Gm. of a reddish brown semi-solid residue. The residue was refluxed on a water bath with 28 cc. of methyl alcohol and 0.7 cc. of concentrated sulphuric acid for 5 hours, and then the excess methyl alcohol was removed. The residue was taken up in ether, the ethereal solution was washed with water to remove the sulphuric acid, then the ethereal solution was dried and the ether removed. The remaining liquid methyl esters were distilled under a pressure of 10 mm. of mercury. A negligible amount of distillate came over between 173° and 189° C.; about 5 cc. of distillate came over at 190° C.; and a small amount of distillate came over between 191° and 215° C. The latter distillate, which was collected separately, was discarded. The distillate which had been collected between 173° and 190° C. was refluxed on a water bath with 10 per cent sodium hydroxide in 70 per cent alcohol for 2 hours. The saponified solution was shaken with ether to remove any unsaponified oil and liberated substances other than the acids. The aqueous solution was then acidified with diluted sulphuric acid and was extracted repeatedly with ether. The ethereal solution was washed with water, dried with anhydrous sodium sulphate, the solvent removed and the solid residue was taken up in warm alcohol. The first crop of crystals, weighing 0.1 Gm., obtained at room temperature melted at 58.5° C. The silver salt was prepared and analyzed.

0.0413 Gm. of salt gave on ignition 0.0124 Gm. of Ag
Ag = 30.0 per cent
$C_{16}H_{31}O_2Ag$ requires Ag = 29.7 per cent.

The compound was very likely palmitic acid with a small amount of impurity.

The mother-liquor was concentrated and kept at 10° C. The solid (2.0 Gm.) which separated was removed, and after recrystallization from alcohol melted at 62–62.5° C. The silver salt was prepared and analyzed.

0.1010 Gm. of salt gave on ignition 0.0308 Gm. of Ag
Ag = 30.0 per cent
$C_{16}H_{31}O_2Ag$ requires Ag = 29.7 per cent
The acid melts at 62–62.5° C.
$C_{16}H_{32}O_2$ melts at 62.6° C.
The methyl ester was collected at 190° C. (10 mm.)
$C_{16}H_{31}O_2CH_3$ boils at 196° C. (15 mm.)
0.0596 Gm. of the acid required 2.34 cc. of 0.1*N* KOH; corresponding to 220.3 mg. of KOH per Gm. of acid
$C_{16}H_{32}O_2$ has a neutralization value of 219.1 mg. of KOH per Gm. of acid
Molecular weight determined from the acid value is 253.9
$C_{16}H_{32}O_2$ = 256.34.

The above-described compound was thus identified as palmitic acid.

The mother-liquor was concentrated and kept at 10° C. A crop of crystals (1.0 Gm.) was obtained, which, after recrystallization from ethyl acetate, melted at 61–62° C. This, undoubtedly, was a further yield of palmitic acid.

The mother-liquor was found to react readily with bromine. The alcohol was removed, leaving a residue which was liquid at room temperature and which solidified when kept at 10° C. The liquefied substance gave a positive elaidin reaction when treated with concentrated nitric acid and copper wire. The silver salt was prepared and analyzed.

0.1756 Gm. of salt gave on ignition 0.0503 Gm. of Ag
Ag = 28.6 per cent
$C_{18}H_{33}O_2Ag$ requires Ag = 27.7 per cent.

Methyl oleate distils at about the same temperature as methyl palmitate.

The above-described residue probably consisted mainly of oleic acid together with some acid or acids which had not been removed by fractionation.

SUMMARY AND CONCLUSIONS.

1. The fatty oil obtained by extracting dried poke root with petroleum benzin was found to have the following constants: Specific gravity$^{25°}_{25°}$ = 0.9209; optical rotation, $[\alpha]^{26°}_{D}$ = +13°; refractive index, $N^{26°}_{D}$ = 1.4741; acid number, 71.97; saponification number, 139.43; ester number, 67.46; iodine number, 69.14.

2. Chemical investigation of the fatty oil proved it to be a complex mixture containing a large proportion of free fatty acids, some esters of fatty acids with glycerol, and wax-like esters of fatty acids with a sterol.

(*a*) A sterol-like compound, $C_{23}H_{40}O$, melting at 107–108° C.; and having an optical activity of $[\alpha]^{26°}_{D}$ = +70.0°, was isolated. The oxygen present in the molecule does not behave as a part of a free hydroxyl group, since boiling with acetic anhydride and with acetyl chloride had no effect on the compound.

(*b*) A sterol (phytolaccasterol), $C_{30}H_{50}O \cdot H_2O$, melting at 169–170° C., and having an optical activity of $[\alpha]^{26°}_{D}$ = +35.0°, was isolated. It is isomeric with the amyrins isolated by Tschirch and Cremer (4), but the differences in the behavior of the acetates prove them to be dissimilar. Phytolaccasterol was proved to be a monohydroxy compound by the saponification of its acetate, from which procedure a molecular weight of 458.4 was calculated as compared with 468.4 as determined by analysis.

(*c*) A hydrocarbon, hentriacontane ($C_{31}H_{64}$), was isolated and identified by its manner of separation and by its inactivity with chemical reagents, and its melting point of 67.4° C.

(*d*) The following fatty acids were isolated: Arachidic, 5.91 per cent; palmitic, 8.63 per cent; margaric, 4.19 per cent; oxymyristic, 0.72 per cent. The presence of oleic acid, acids of low molecular weight and glycerol was proved.

REFERENCES.

(1) Lewkowitsch, J., "Chemical Technology and Analysis of Oils, Fats and Waxes," 1, 276 (1921).
(2) Lewkowitsch, J., *Ibid.*, 1, 275 (1921).
(3) Boemer, A., *Ztschr. Untersuch. Nahres. Genussm.*, 1, 21 (1898).
(4) Tschirch and Cremer, *Arch. Pharm.*, 240, 293 and 322 (1902).
(5) Vesterberg, *Ber.*, 20, 1242 (1887).

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1935–1936.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 23.

June 17, 1936.

To the Members of the Council:

147. Use of Text of N. F. VI. Motion No. 67 (Council Letter No. 22, page 555) has been carried and Lea & Febiger have been so advised.

The following letters have been received from Chairman DuMez of the Committee on Publications:

> "The request from William Wood & Company for permission to quote portions of the National Formulary VI in a revised edition of Stedman's Practical Medical Dictionary, is one of a type which it has been our custom to grant. I therefore recommend that the Council grant permission to William Wood & Company to use portions of the text of the N. F. VI in the revision of Stedman's Practical Medical Dictionary."
>
> "Inasmuch as the request of W. H. Blome to use portions of the text of the N. F. VI in the revision of Washburn's and Blome's textbook on pharmacognosy and materia medica does not involve any new features, I recommend that permission be granted and that the payment of the fee previously charged, namely, $5.00, be again required."

(*Motion No. 70*) It is moved by DuMez that William Wood & Co. and Washburn and W. H. Blome be granted permission to use the text of the N. F. VI in a revised edition of Stedman's Practical Medical Dictionary and in a revised edition of a textbook on Pharmacognosy and Materia Medica, respectively, with the customary acknowledgment and the usual fee of $5.00 in each case.

148. Request for Additional Compensation on Account of Printing and Binding the N. F. VI. Motion No. 66 (Council Letter Nos. 21 and 22, pages 472 and 555) has been carried and the Mack Printing Company will be paid the amount requested.

149. Committee on Pharmacy Week. Two members of the Council have sent in comments on the recommendations as submitted with Council Letter No. 22. Other members who wish to submit comments are requested to do so promptly in order that a decision may be reached.

150. Election of Members. Motion No. 69 (Council Letter No. 22, page 556) has been carried and applicants for membership numbered 350 to 360, inclusive, are declared elected.

151. Applicants for Membership. The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 361, Thomas Lloyd Barnhart, 316 Mills Ave., Braddock, Penna.; No. 362, Edward Bardell Yeager, 2300 Arlington Ave., Carrick, Pittsburgh, Pa.; No. 363, Angelus Edward Rihn, 936 Fifth Ave., Ford City, Pa.; No. 364, E. Alfonso Singleton, 319 N. 2nd St., Reading, Penna.; No. 365, Ora H. Ellis, 124 Des Moines St., Des Moines, Iowa; No. 366, R. A. Kramer, 147 Waverly Place, New York, N. Y.; No. 367, Selwyn George Davis, 5357 Santa Monica Blvd., Hollywood, Calif.; No. 368, J. Louis Lanz, 6300 Etzel Ave., St. Louis, Mo.; No. 369, J. B. Whitney, Jr., 32–16 Gellhall Plaza, Kansas City, Mo.; No. 370, Hugo Mock, 10 E. 40th St., New York, N. Y.; No. 371, Robert R. Pierce, 457 High St., Morgantown, W. Va.; No. 372, Lynn L. Carson, 700 Charles St., Wellsburg, W. Va.; No. 373, Gaylord Hess Dent, 130 Fayette St., Morgantown, W. Va.; No. 374, E. Guy Robertson, 840 13th Ave., Huntington, W. Va.; No. 375, Harry Alan Goodykoontz, 906 Raleigh Terrace, Bluefield, W. Va.; No. 376, Percy S. Walker, 201 W. 6th Ave., Topeka, Kans.; No. 377, Gune Krishna Gangadhar, Court Road, Ahmednagar, Bombay, India;

No. 378, Rudolph Schiffmann Steward, 1734 N. Main St., Los Angeles, Calif.; No. 379, Hans Johann van Giffen, No. 9 Vondelstraat, Amsterdam, Holland; No. 380, James Vans MacDonald, 929 W. Georgia, Vancouver, B. C., Canada; No. 381, J. Otto Kohl, McMicken Ave. and Mohawk Pl., Cincinnati, Ohio; No. 382, Raul Arturo Trillo, 236 Lewis St., Memphis, Tenn.; No. 383, Gail Albert Wiese, Anita, Iowa; No. 384, Charles T. Longo, 410½ Clinton St., Brooklyn, N. Y.; No. 385, Tarvin A. Hoops, Powell, Wyo.; No. 386, Frederick A. Fuhrman, Coquille, Ore.; No. 387, Albert Rice, 1032 N. Parkside Ave., Chicago, Ill.; No. 388, Marvin Klopsch Schroeder, 810 Cedar St., Michigan City, Ind.; No. 389, Milton Robert Hillman, 200 Goffe Terrace, New Haven, Conn.; No. 390, Bessie Maybelle Copper, McDonald, Kans.; No. 391, Robert Gordon Hiler, 616 Church St., Ann Arbor, Mich.; No. 392, Louis Landau, 2718 Glendale Ave., Detroit, Mich.

(*Motion No. 71*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

E. F. KELLY, *Secretary*.

LETTER NO. 24.

July 6, 1936.

To the Members of the Council:

152. Use of Text of N. F. Motion No. 70 (Council Letter No. 23) has been carried and William Wood & Co., and W. H. Blome have been advised:

> "In response to the request contained in your letter of the 20th, it is recommended that permission be granted to P. Blakiston's Son & Co., Inc., to use portions of the text of the N. F. VI for comment in the Second Edition of Muldoon's 'Text Book of Organic Chemistry' and that the customary fee of $5.00 be charged for this grant."
>
> "In response to the request contained in the letter of G. A. Bender of the N. A. R. D. it is recommended that permission be granted to the N. A. R. D. to use portions of the N. F. VI for comment in a revision of the booklet entitled 'Some Important U. S. P. and N. F. Preparations.' It is further recommended that no fee be charged for this grant."

(*Motion No. 72*) It is moved by DuMez that P. Blakiston's Son & Co. and the National Association of Retail Druggists be granted permission to use the text of the N. F. VI in the second edition of Muldoon's "Text Book of Organic Chemistry" and in a revised edition of "Some Important U. S. P. and N. F. Preparations," respectively, with the customary acknowledgment, in each case, and the usual fee of $5.00 in the first case.

153. Election of Members. Motion No. 71 (Council Letter No. 23) has been carried and applicants for membership numbered 361 to 392, inclusive, are declared elected.

154. Applicants for Membership. The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 393, Carl W. Noren, 2019 E. Lake St., Minneapolis, Minn.; No. 394, Samuel Isermann, 57 Wilkinson Ave., Jersey City, N. J.; No. 395, Elmer E. Chilson, 294 Pearl St., Rochester, N. Y.; No. 396, Frank S. Houck, Gloversville, N. Y.; No. 397, Arthur F. Anderson, 16 S. Main St., Minot, N. Dak.; No. 398, Elder G. Otis, Abercrombie, N. Dak.; No. 399, John Whalen, Langdon, N. Dak.; No. 400, Erick Kather, 212 Main St., Williston, N. Dak.; No. 401, S. L. Mark, 118 Fifth Ave. So., Jamestown, N. Dak.; No. 402, H. F. Easton, Crosby, N. Dak.; No. 403, Geo. J. Holicky, 414 Main St., Breckenridge, Minn.; No. 404, Homer L. Hill, Towner, N. Dak.; No. 405, Geo. C. Benno, 108 S. Main St., Minot, N. Dak.; No. 406, Samuel M. Dripps, 324 5th St., Elizabeth, Pa.; No. 407, Richard A. Rhone, 26 Edna Ave., Bradford, Pa.; No. 408, Joseph Albert Meisner, 1069 Norwich Ave., Pittsburgh, Pa.; No. 409, John Stanley McAleer, 5210 Gertrude St., Pittsburgh No. 7, Pa.; No. 410, Isadore Browarsky, State St., Oakdale, Pa.; No. 411, Norman J. Ilkuvitz, 553 Miller Ave., Clairton, Pa.; No. 412, Willard H. Roberts, 230 Genesee St., Utica, N. Y.; No. 413, John Joseph Gill, 5706 Harper Ave., Chicago, Ill.; No. 414, Charles F. Boesel, 8616 Trafford Lane, St. Louis, Mo.; No. 415, Paul Eric Sick, Calle Belgrano 3655, Buenos Aires, Argentina; No. 416, Henry J. Gillen, 38 Fabyan St., Dorchester, Mass.; No. 417, Ella Lehrman,

15 Woolson St., Mattapan, Mass.; No. 418, Otto H. Anderson, 87 Arlington St., Fitchburg, Mass.; No. 419, Benjamin P. Hecht, 70 Wildwood St., Mattapan, Mass.; No. 420, Frank Shinopulos, 105 Pleasant St., Dorchester, Mass.; No. 421, Clara D. Herskowitz, 4900 Riestertown Rd., Baltimore, Md.; No. 422, Loyd Debert Carroll, 1408 N. Alabama St., Indianapolis, Ind.; No. 423, Mary Nancy Pike, 2 S. Union St., Concord, N. Car.; No. 424, Ernest Royce, Napa State Hospital, Imola, Calif.; No. 425, Arthur R. Cade, 607 Fifth Ave., So., Minneapolis, Minn.; No. 426, Lorenz Harrd Jensen, 1977 So. Huron St., Denver, Colo.; No. 427, Milton Laughland, 133 Sagamore Rd., Apt. 9*B, Tuckahoe, N. Y.; No. 428, Noble C. Earl, c/o United Drug Co., Boston, Mass.; No. 429, Charles L. Pickens, 626 McDonough Blvd. S.E., Atlanta, Ga.; No. 430, Robert G. Eberhard, 15 E. 40th St., New York, N. Y.; No. 431, H. P. Lundin, Watford City, No. Dak.; No. 432, Cap. H. Saunders, Minot, N. Dak.; No. 433, Yeikuma Koba, Doshou machi 3 chome, Osaka, Japan.

(*Motion No. 73*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

155. Use of Text of N. F. VI. The following letters have been received from Chairman DuMez of the Committee on Publications:

> "Inasmuch as Dr. Henry Kraemer was granted permission to use portions of the text of the N. F. V for comment in his 'Text Book on Pharmacognosy,' it is recommended that permission be granted to Professors Gathercoal and Wirth to use portions of the text of the N. F. VI in the preparation of a textbook on pharmacognosy to be patterned after the one prepared by Dr. Kraemer and that the customary fee of $5.00 be charged."
>
> "Inasmuch as Lea and Febiger were granted permission to use portions of the text of the N. F. V for comment in 'Cushny's Pharmacology and Therapeutics,' it is recommended that permission be granted them to use portions of the text of the N. F. VI for the same purpose and that the customary fee of $5.00 be charged for this purpose."

(*Motion No. 74*) It is moved by DuMez that E. N. Gathercoal and E. H. Wirth and Lea and Febiger be granted permission to use portions of the text of the N. F. VI in a new textbook on Pharmacognosy and in a revision of Cushny's Pharmacology and Therapeutics by Edmunds, respectively, with the customary acknowledgment and at the usual fee of $5.00 in each case.

156. Tentative General Program for the Eighty-Fourth Annual Meeting. With the approval of President Costello, Local Secretary Adams and the Committee on Standard Program of the Council, the secretary submits the attached tentative general program. Officials of the various affiliated organizations represented in the program have approved those features in which their respective organizations are directly interested.

The changes suggested in the tentative program for the 1936 meeting are:

(*a*) The meeting of the Council has been scheduled for Sunday.

(*b*) The First Session of the Conference of Law Enforcement Officials has been scheduled for Monday evening, August 24th, at the request of the officers of the Conference.

(*Motion No. 75*) It is moved by Kelly that the tentative general program of the Eighty-Fourth Annual Meeting be approved. A vote on this motion will be called for in about one week.

E. F. KELLY, *Secretary.*

GENERAL PROGRAM FOR THE EIGHTY-FOURTH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AND AFFILIATED ORGANIZATIONS, HOTEL ADOLPHUS, DALLAS, TEXAS, AUGUST 24–29, 1936.

All dates included in special fare arrangements. All meeting rooms for business sessions located on the Fifth and Sixth Floors and are air-conditioned.

AUGUST 17TH–21ST.

Plant Science Seminar. Program, see A. PH. A. JOURNAL, June, page 568. Meetings will be held at the State Park and Game Preserve, near Wilburton, Okla.

SATURDAY, AUGUST 22ND.

2:00 P.M. National Conference on Pharmaceutical Research—Ball Room.
8:00 P.M. National Conference on Pharmaceutical Research—Ball Room.

SUNDAY, AUGUST 23RD.

9:30 A.M. Council, A. PH. A.—Parlor D.
8:00 P.M. American Council on Pharmaceutical Education—Parlor B.

MONDAY, AUGUST 24TH.

9:00 A.M. N. A. B. P.—Ball Room.
9:00 A.M. A. A. C. P.—Executive Committee—Parlor E.
9:00 A.M. A. A. C. P.—Teachers' Conferences.

Chemistry Conference—Ball Room.
Pharmacy Conference—Texas Room.
Pharmacognosy and Pharmacology Conference—Parlor A.
Pharmaceutical Economics Conference—Parlor B.

2:00 P.M. N. A. B. P.—Ball Room.
2:00 P.M. A. A. C. P.—Texas Room.
6:00 P.M. Dinner, N. A. B. P.—Palm Garden.
6:00 P.M. Dinner, A. A. C. P.—Danish Room.
8:00 P.M. A. A. C. P.—Texas Room.
8:00 P.M. First Session Conference Law Enforcement Officials—Parlor A.
10:00 P.M. Reception—(Informal) followed by dancing—Ball Room.

TUESDAY, AUGUST 25TH.

9:00 A.M. Joint Meeting N. A. B. P. and A. A. C. P.—Ball Room.
12:15 P.M. Luncheon, Committee on National Formulary—Parlor B.
1:30 P.M. First Session, House of Delegates—Ball Room.
2:30 P.M. N. A. B. P.—Ball Room.
2:30 P.M. A. A. C. P.—Texas Room.
6:30 P.M. Joint Banquet, A. PH. A. and Related Organizations—Ball Room.

WEDNESDAY, AUGUST 26TH.

9:00 A.M. First General Session, A. PH. A.—Ball Room.
12:15 P.M. Luncheon, Syllabus Committee—Parlor D.
2:00 P.M. First Session, Scientific Section—Ball Room.
2:00 P.M. First Session, Section on Education and Legislation—Texas Room.
2:00 P.M. First Session, Section on Commercial Interests—Parlor A.
2:00 P.M. First Session, Section on Historical Pharmacy—Parlor B.
2:00 P.M. First Session, Conference of Pharm. Asso. Secretaries—Parlor C.
3:00 P.M. Meeting Committee on Nominations—Parlor E.
6:00 P.M. Dinner, Rho Chi Fraternity followed by Annual Convention—Danish Room.
8:00 P.M. Second Session, House of Delegates—Ball Room.

THURSDAY, AUGUST 27TH.

9:00 A.M. Council A. PH. A.—Parlor D.
9:00 A.M. Second Session, Section on Commercial Interests—Parlor A.
9:00 A.M. Second Session, Scientific Section—Ball Room.
9:00 A.M. First Session, Section on Practical Pharmacy & Dispensing—Parlor C.
9:00 A.M. Second Session, Section on Historical Pharmacy—Parlor B.
9:00 A.M. Second Session, Conference of Law Enforcement Officials—Texas Room.
12:00 M. Veteran Druggists' Luncheon—Palm Garden.
2:00 P.M. Second General Session, A. PH. A.—Ball Room.
6:00 P.M. Dinner, Kappa Psi Fraternity and Lambda Kappa Sigma Sorority—Palm Garden.
6:00 P.M. Dinner, Phi Delta Chi Fraternity—Danish Room.

8:00 P.M. Joint Session, Scientific Section & Section on Practical Pharmacy and Dispensing—Ball Room.
8:00 P.M. Joint Session, Section on Education and Legislation, Conference of Pharmaceutical Law Enforcement Officials, and Conference of Pharmaceutical Association Secretaries—Texas Room.
8:00 P.M. Meeting, Committee on Resolutions—Parlor B.

FRIDAY, AUGUST 28TH.

9:00 A.M. Third Session, Scientific Section—Ball Room.
9:00 A.M. Second Session, Section on Practical Pharmacy and Dispensing—Parlor C.
9:00 A.M. Second Session, Section on Education and Legislation—Texas Room.
9:00 A.M. Second Session, Conference of Pharm. Asso. Secretaries—Parlor A.
1:00 P.M. Meeting, Committee on Resolutions—Parlor A.
2:00 P.M. Final Session, House of Delegates—Ball Room.
6:00 P.M. Dinner, Former Presidents, A. PH. A.—Parlor A.
6:00 P.M. Special Dinners.
8:00 P.M. Final General Session, A. PH. A.—Ball Room.
10:00 P.M. Farewell Party—Ball Room.
10:00 P.M. Council A. PH. A.—Parlor D.

SATURDAY, AUGUST 29TH.

9:30 A.M. Entertainment—Arrangements to be announced later.

NOTICE FROM THE TRANSPORTATION COMMITTEE.

Very favorable rates are in effect this summer from all parts of the United States and Canada to Dallas and return to the starting point, on account of the Texas Centennial Exposition. In general, round trip rates are about one and one-third of the new low one-way fares, and the tickets are good for thirty days. Also, subject to the usual restrictions, diverse routes may be used for the going and returning journeys. These reduced rate tickets are on sale at all important railroad stations, and their low cost is shown in the list below, giving the round-trip rates for some widely scattered cities. These "first-class" fares are for Pullman cars and the cost of berths or seats must be added to them. Up to the present time, we have been unable to secure the special rates from certain stations in the northeast and the far west, but we are assured that they are correspondingly low. All or nearly all Pullman cars on southern runs are air-conditioned.

While we believe that these rates are correct, their accuracy cannot be guaranteed. Coach fares are still lower than the following rates.

Albany, N. Y.	$67.25	Memphis, Tenn.	$18.75
Asheville, N. C.	40.90	Milwaukee, Wis.	40.55
Atlanta, Ga.	33.55	Mobile, Ala.	25.10
Boston, Mass.	79.35	Montreal, Que.	87.15
Buffalo, N. Y.	61.85	New York, N. Y.	67.25
Charleston, S. C.	44.25	Omaha, Nebraska	27.80
Chicago, Ill.	38.20	Pittsburgh, Pa.	56.05
Cincinnati, Ohio	38.75	Portland, Me.	87.05
Cleveland, Ohio	54.05	Providence, R. I.	78.45
Columbus, Ohio	45.95	Richmond, Va.	53.95
Denver, Colo.	33.25	St. Louis, Mo.	26.70
Des Moines, Ia.	29.05	St. Paul, Minn.	39.10
Detroit, Mich.	52.50	Salt Lake City, U.	52.20
Indianapolis, Ind.	38.75	Toledo, Ohio	49.40
Kansas City, Mo.	19.80	Toronto, Ont.	66.45
Louisville, Ky.	33.95	Washington, D. C.	56.05

Information about the post-convention tour through Southern Texas and Mexico to Mexico City, which is being arranged, may be obtained from Sam P. Harben, 512 Allen Building, Dallas, Texas.

THEODORE J. BRADLEY, *Chairman*, Committee on Transportation, A. PH. A.

HOTEL ADOLPHUS—HEADQUARTERS.

The meeting rooms to be used by the AMERICAN PHARMACEUTICAL ASSOCIATION are air-conditioned.

The rates of a number of hotels are given, together with the number of rooms and the names of the managers. If you desire, make inquiry relative to air-condition or other comforts.

Hotel Adolphus.

Hotel.	Address.	Rooms.	Rates, Single.	Rates, Double.	Manager.
Adolphus	Commerce-Akard-Main	825	$2.50 to $5.00	$4.00 to $7.00	H. Fuller Stevens
Ambassador	1312 S. Ervay	300	3.00 to 5.00	3.50 to 6.00	C. A. Sheffield
Baker	Commerce-Akard	700	2.50 to 5.00	4.00 to 7.00	Fenton J. Baker
Bluebonnet	1302 Commerce	150	1.50 to 3.50	2.50 to 5.00	Dean Carpenter
Campbell	Elm-Harwood	108	1.00 to 2.00	1.50 to 3.00	George C. Scott
Ervington	Ervay & Pocahontas	250	2.50 to 5.00	3.50 to 10.00	W. D. Reaves
Hilton	Main-Harwood	320	1.50 to 3.00	2.50 to 6.00	C. C. Rank
Jefferson	Wood-Jefferson-Houston	450	1.50 to 6.00	2.50 to 8.00	Lawrence Mangold
Mayfair	723 N. St. Paul	150	1.50 to 2.50	2.50 to 4.00	Jack W. Tucker
Sanger Apartments	Ervay at Canton	325	2.00 to 5.00	3.00 to 7.00	Mr. & Mrs. Ted Spreng
Southland	Main-Murphy-Commerce	250	1.50 to 3.00	3.00 to 5.00	Joe Hallaman
Texan	Jackson & Houston	60	1.50 to 2.50	2.50 to 4.00	C. A. & H. W. Russell
Whitmore	Commerce-Martin	125	2.00 to 5.00	3.50 to 10.00	Curtis F. Reach
Worth	1014 Main	75	1.00 to 2.00	1.50 to 3.50	F. R. Singletary

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CHAIRMEN, DALLAS A. PH. A. CONVENTION COMMITTEES.

Left to Right: *Membership Committee*, B. B. Brown; *Local Secretary*, Walter D. Adams; *Reception Committee*, H. C. Burroughs; *Women's Auxiliary Committee*, Mrs. R. M. Walmsley; *Convention Committee*, E. C. Harrell; *Treasurer*, W. E. Hill; *N. A. B. P. Arrangements*, W. H. Cousins; *V.-C., Reception Committee*, B. E. Hazard; *Entertainment Committee*, M. H. White.

A. PH. A. LOCAL BRANCHES

Secretaries will please report incorrections and elections. Also render reports of meetings. Thank you.

BALTIMORE.
No fixed meeting night.
President, A. N. Hewing.
Vice-President, Chas. S. Austin, Jr.
Secretary-Treasurer, Robert S. Fuqua.
Chairmen of Committees: Membership, Gilbert Josephs; Professional Relations, Marvin J. Andrews; Science and Practice of Pharmacy, Samuel L. Fox; Education and Legislation, A. G. DuMez.

STUDENTS AUXILIARY, MARYLAND UNIVERSITY, SCHOOL OF PHARMACY.
President, P. H. Thompson.
First Vice-President, J. R. Karns.
Second Vice-President, W. Gakenheimer.
Secretary, S. Glickman.
Treasurer, R. Thompson.
Editor, R. V. Robinson.
Executive Committee: A. Tramer, G. A. Mouat, G. Kelley, M. R. Thompson, Frank J. Slama.

CHICAGO.
Meet third Tuesday.
President, S. W. Morrison.
First Vice-President, H. M. Emig.
Second Vice-President, R. A. G. Linke.
Third Vice-President, O. U. Sisson.
Secretary-Treasurer, L. Templeton.
Delegate to the House of Delegates, L. Templeton.
Committee Chairmen: Membership, Thomas F. Rylands; Legislation, J Riemenschneider; Practice, I. A. Becker; Medical Relations, Dr. Bernard Fantus; Publicity, A. E. Ormes.

CINCINNATI.
Meet second Tuesday.
President, C. W. Sondern.
Vice-President, T. H. Rider.
Secretary, R. L. Puls.
Treasurer, John P. Jennie.
Delegate to the House of Delegates, A. Ph. A., Frank H. Freericks.
Trustees: C. G. Merrell (1937), B. J. Kotte (1936), Nicholas Blank (1935), Frank H. Freericks (1934), Bertha M. Ott (1933).

DETROIT.
Meet third Thursday.
President, Berton Todd.
First Vice-President, Carl Novak.
Second Vice-President, Lawrence Main.
Secretary, Bernard A. Bialk.
Treasurer, Frederick F. Ingram.
Student Council, Hamilton Whitman and Florence Hartsoff, U. of M.; Henry Tyszka and William Hennesy, D. I. T.; Berton Todd and William Blatchley, C. C. D.; *Council of Clerks*, Robert Woonsocket, U. of M.; Douglas Robinson, D. I. T.; James Lidell, C. C. D.; *Secretary*, Bernard A. Bialk; *Treasurer*, Fred Ingram; *Chairman, Program Committee*, R. T. Lakey.

NEW YORK.
Meet second Monday.
President, Frederick C. A. Schaefer.
Vice-President, Otto F. A. Canis.
Secretary, Horace T. F. Givens.
Treasurer, Turner F. Currens.
Delegate to the House of Delegates, Hugo H. Schaefer.
Secretary, Remington Honor Medal Committee, Hugo H. Schaefer.
Chairmen of the Committees: Education and Legislation, Robert S. Lehman; Progress of Pharmacy, Leonard W. Steiger; Professional Relations, James H. Kidder; Audit, Ernst A. Bilhuber; Membership, Rudolf O. Hauck.

NORTHERN NEW JERSEY.
President, George C. Schicks.
Vice-President, Robert W. Rodman.
Secretary, C. L. Cox.
Treasurer, A. F. Marquier.

NORTHERN OHIO.
President, Ellsworth Loesch.
Vice-President, F. W. Gehring.
Secretary, Neil T. Chamberlin.
Treasurer, Herbert Decker.

NORTH PACIFIC.
President, Fred. A. Geue.
First Vice-President, George Haack.
Second Vice-President, M. Frederick Grill.
Secretary-Treasurer, Harvey J. Donnell.
Chairmen of Committees: Practical Pharmacy, Harry Weis; Professional Relations, L. G. Haack; Programs, Earl Gunther; Membership, Frank Nau.

NORTHWESTERN.
President, R. Almin.
Secretary-Treasurer, C. V. Nets.

PHILADELPHIA.
President, L. L. Miller.
First Vice-President, H. Evert Kendig.
Second Vice-President, S. H. Kerlin.
Secretary-Treasurer, George E. Byers.
Chairman of Committees: Professional Relations, W. A. Pearson; Practical Pharmacy, Ambrose Hunsberger; Membership, S. H. Kerlin; Entertainment, Prof. Adley B. Nichols.
Delegate to the House of Delegates, Ambrose Hunsberger.

PITTSBURGH.
Meet third Tuesday.
President, Edward C. DeBone.
Vice-President, W. Gordon Sleigh.
Secretary-Treasurer, Frank S. McGinnis.
Delegate to the House of Delegates, C. Leonard O'Connell.

UNIVERSITY OF CALIFORNIA STUDENT BRANCH.
President, John Doble.
Vice-President, Raymond R. Guehring.
Secretary, Elsie H. Bennetts.
Treasurer, Everett S. Ostrom.
Student Council Representative, Harold Rolph Hefner.
Student Director of Drug Garden, Gleb Al. Popoff.

UNIVERSITY OF SOUTHERN CALIFORNIA, STUDENT BRANCH.
President, Harold Miller.
Honorary President, Albert Musick.
Vice-President, David Ostrom.
Secretary, Masaru Masuoka.
Treasurer, Ernest Yamaguchi.
Faculty Advisers, Harold R. Bowers and Alvah G. Hall.

UNIVERSITY OF FLORIDA, STUDENT BRANCH.
President, C. Herbert Gilliland.
Vice-President, Robert L. White.
Secretary, Robert Gerald Goedhart.
Treasurer, Paul Fehder.

UNIVERSITY OF NORTH CAROLINA, STUDENT BRANCH.
President, L. G. Barefoot.
First Vice-President, D. B. Forrest.
Second Vice-President, C. B. Clark, Jr.
Secretary-Treasurer, H. M. Dellinger.

STUDENT BRANCH, PITTSBURGH COLLEGE OF PHARMACY.
President, Joseph A. Meisner.
Vice-President, Chester A. Krause.
Secretary, Wm. B. Strothman.
Treasurer, Wilbur B. Grove.

SOUTH DAKOTA STATE COLLEGE, STUDENT BRANCH.
President, Frederick J. Ahlfs.
Vice-President, Stanford Maresh.
Secretary, Eugene C. Kuske.
Treasurer, Charles F. Buck.

STUDENT BRANCH, STATE COLLEGE OF WASHINGTON.
President, Leonard Zagelow.
First Vice-President, Ted Stahlborn.
Second Vice-President, Gail Howard.
Secretary-Treasurer, Belle Wenz.
Reporter, Harold Freed.

ST. JOHN'S UNIVERSITY STUDENT BRANCH.
President, Saul Asnis.
Vice-President, Isidore J. Berman.
Treasurer, John E. Graziano.
Secretary, Isabelle Seissman.

UNIVERSITY OF WISCONSIN, STUDENT BRANCH.
President, George Vosmek, Antigo.
Vice-President, George I. Schefelker, Stoughton.
Secretary, Norman Glander, Manitowoc.
Treasurer, Arnie Stensby, Stoughton.
Adviser, Edward J. Ireland.

OKLAHOMA UNIVERSITY PHARMACEUTICAL ASSOCIATION.
Meet every Friday morning at 10:00 o'clock, during the school year.
President, Bill Cates Atoka.

Honorary President, Val Adams, Oklahoma City.
Vice-President, Frank Ozment, Jr., Talihina.
Secretary, Katherine Searle, Redrock.
Treasurer, Jerry Gwin, Ada.
Chairman of the Program Committee, J. Pat Henry, Ringling.
Chairman of the Committee on Public Relations, E. E. Parsons, Okemah.
Chairman of the Committee on Sports, Gene McGill, Alva.

LOUISVILLE COLLEGE OF PHARMACY STUDENT BRANCH.
President, William J. Walsh.
Vice-President, Fred P. Kranz, Jr.
Secretary, Joe Black.
Treasurer, John M. Burton.
Faculty Adviser, Dean G. L. Curry.
Program Committee: *Chairman*, Horace Hannon, Sister Crescentia Wise, Henry J. Zurlage.
Student Activities Committee: *Chairman*, Claude M. Lloyd; Sister Margaret Ann Schwering, Edward E. Krebs.
Membership Committee: *Chairman*, Fred P. Kranz, Jr.; Hal F. Acuff, Joe P. Forgy, Jr.

UNIVERSITY OF MISSISSIPPI STUDENT BRANCH.
President, J. W. Duckworth.
Vice-President, Tony Rosetti.
Secretary, J. M. Longmire.
Treasurer, W. J. Hossley, Jr.
Faculty Adviser, Prof. W. W. Johnson.

PRELIMINARY REPORT OF THE COMMITTEE TO STUDY THE BY-LAWS OF THE ASSOCIATION.

Subsequent to the annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION at Portland, President Costello appointed a Committee to Study the Constitution and By-Laws, as such a group was recommended by the Portland convention, and grew out of certain recommendations made by Doctor Robert P. Fischelis in his presidential address.

The Committee was requested to apprise the membership in advance of the annual meeting of the changes proposed.

The recommendations in the address of President Fischelis, which were referred to the Committee for study, read as follows:

Recommendations Nos. 2, 5 and 13.

(2) It is recommended that the secretary of the ASSOCIATION be also designated as general manager, and that this title shall carry with it executive supervision of and responsibility for the activities of the ASSOCIATION in the headquarters building.

(5) It is recommended that the president-elect be made an ex-officio member of the Council immediately following his election, and that the procedure at the annual convention be so arranged as to give the president-elect an opportunity to submit recommendations in time for approval at the meeting at which he takes office.

(13) It is recommended that the By-Laws be amended to reduce membership of the Council to six elected members and three ex-officio members, namely: The President, the President-Elect and the Chairman of the House of Delegates. The six elected members should be distributed geographically in accordance with the concentration of membership.

In this connection, it will also be recalled that Robert L. Swain, in his presidential address the year preceding, recommended that the number of nominees for the presidency of the ASSOCIATION, as well as the number nominated for first vice-president and second vice-president, be reduced from three to two, and that the immediate past-president serve as an ex-officio member of the Council for the year following his term of office.

These recommendations have been met in the following proposed changes in the By-Laws. Omitted words are in parenthesis, and newly added words are *underlined*.

CHAPTER I.

ELECTION OF OFFICERS AND MEMBERS OF THE COUNCIL.

Article I. Nomination of President, Vice-Presidents and Councilors. The House of Delegates shall at its second session, held during the annual meeting of the ASSOCIATION, nominate by ballot (three) *two* candidates, one of whom shall be, as hereinafter provided, elected President to serve for one year; (three) *two* candidates for First Vice-President, one of whom shall be elected for one year; (three) *two* candidates for Second Vice-President, one of whom shall be elected for one year; and nine candidates, three of whom shall be, as hereinafter provided, elected members of the Council to serve for three years.

The Council is empowered and directed to fill all vacancies in the list of nominees, which occur by death or resignation, after the adjournment of the annual meeting of the Association and prior to the issuance of mail ballots.

CHAPTER II.

Article I. President. Last line of Article I shall read as follows: He shall be (an ex-officio) *a* member of the Council.

The following sentence is added to Article III.

The Secretary shall also serve as General Manager of the Association, and shall have executive supervision over its activities, including direction of and responsibility for the headquarters building and the activities of the Association carried on therein.

CHAPTER III.

COUNCIL.

Article I. Membership. The Council shall consist of (17) *19* members, each of whom has held membership in the ASSOCIATION for five years or more and (no one of whom is an officer of the House of Delegates) elected as hereinbefore provided. The (President), *the immediate Past-President, the President-Elect,* the Vice-Presidents, the Chairman of the House of Delegates, the Editor of the JOURNAL, the Editor of the YEAR BOOK, the Secretary and Treasurer of the ASSOCIATION shall be ex-officio members of the Council. The elected members of the Council shall serve until their successors have been installed.

Within 30 days following the annual meeting of the Association, the Secretary shall call upon the Council to elect by Mail Ballot, three members of the Council, to be chosen from the nine elected members, who, with the Chairman of the Council and the President of the Association, shall constitute an Executive Committee of the Council. The Executive Committee shall confer with the Secretary upon his request, and shall advise with him upon all matters having to do with the affairs and activities of the Association. In all cases, however, the conclusion of the Executive Committee, together with an abstract of its proceedings, shall be submitted to the Council by mail, for ratification or rejection, upon majority vote of the members.

CHAPTER VII.

LOCAL BRANCHES *and Student Branches.*

CHAPTER VIII.

Article I. Standing Committees.

1. Committee on Local *and Student* Branches.
12. *Committee on Pharmacy Week.*
13. *Committee on the Status of Pharmacists in the Government Services.*

The Committee secured legal advice that the Articles of Incorporation did not limit the number of members of the Council.

ROBERT L. SWAIN, *Chairman.*

A. PH. A. RESEARCH AWARD.

The AMERICAN PHARMACEUTICAL ASSOCIATION announces the award of a grant totaling $1000.00 which will be available on October 1, 1936, for research in medicinal substances. In making the announcement, Chairman H. V. Arny, of the Committee on Research of the A. PH. A., requests those desiring aid to write him at 115 W. 68th St., New York City, before August 5th, giving name and laboratory connections, outline of research in contemplation and amount of grant requested.

Dr. Arny points out that present plans call for publication in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION of the paper describing the results of the research.

THE ADVANCEMENT OF SCIENCE.

Special endowment funds give the American Association for the Advancement of Science a limited income which, in accordance with the conditions of the donors, may be used in making small grants to individuals for encouragement in research. Special blanks may be secured from the office of the permanent secretary, Smithsonian Institution Building, Washington, D. C., on which those who desire may make application. It is essential that there be at least two sponsors who are able to speak both of the applicant and of the project from personal acquaintance and are qualified to pass upon the worker and the proposed utilization of the grant.

EDITORIAL NOTES

OLD TEXAS MISSIONS.

Second only to the Alamo as a sacred shrine of Texas martyrdom is the old mission of La Bahia del Espiritu Santo, popularly known as the Mission of Goliad, near the city of Goliad. Here Fannin and his men were held prisoners before their massacre by order of the Dictator, Santa Anna, on March 27, 1836. During Spanish colonial days a presidio or garrison of soldiers was maintained here. Originally located on Matagorda Bay, the mission and presidio were transferred inland to the present site on the San Antonio River about the middle of the eighteenth century.

San José Mission at San Antonio generally is recognized as the finest example of Franciscan mission architecture to be found in the present limits of the United States. Its famous rose window has been the subject of song and legend for many generations. Extensive restoration of the entire mission compound as it was originally laid out by the missionary fathers has been made possible in recent years through Public Works Administration grants.

MEXICAN HIGHWAY.

How important in the Texas program of economic and social development really is the construction of a Mexican highway system, is something that is hard to appreciate fully. It is mentioned here because some of our members contemplate a trip to Mexico City.

THE ARMY MEDICAL LIBRARY.

The Army Medical Library has celebrated its Centennial. It began with a small collection of books placed in the office of Surgeon General Lovell and has now grown to be the largest Medical Library in the world. The beginning of the Library was prompted by Dr. John Shaw Billings because in the writing of his thesis he was unable to find the required references in any one library and it was necessary for him to consult the libraries of various sections of the country. The space occupied by the Army Medical Library, in Washington, during its early years, was so small that in opening cases of books it was necessary to take them outside of the building.

The Library now has nearly 450,000 volumes.

EXHIBIT OF BOOKS.

A collection of books relating to the history of the medical sciences was on exhibit in the Lima Library, Catholic University, and was open to the public for a week. Among the books are "The Drugs and Spices of India," by Garcia da Orta, printed in Goa, India, in 1563. This volume, written in Portuguese, contains one of the earliest descriptions of cholera and its remedy, and through it Europe learned of the plants and botany of the East.

Other books include "A Natural History of Brazil," by William Tiso and George Marcgraf, printed in Amsterdam in 1648, which for over a century was one of the principal scientific works on Brazil, and "History, Natural and Moral of the Indies," by Joseph Acosta, S. J., also a treatise on the pestilence of Pernambuco by John Sarreyra a Rosa, containing one of the first descriptions of yellow fever known in Europe, printed in Lisbon in 1694.

SOCIAL ASPECTS OF SICKNESS.

The Committee on Legislative Activities of the American Medical Association, which is headed by Dr. E. H. Cary, has recently authorized a release to the presidents and secretaries of State associations and delegates to the American Medical Association, in which it stresses the desirability of less discussion of the topic "Medical Economics" and more emphasis upon "Social Aspects of Sickness."

MEDICINE AND MACHINERY.

"To-day we are witnessing the apotheosis of the machine in human life and it is not surprising to find that medicine, like other spheres of action, is being mechanized. The public has come to believe that machinery is revolutionizing the healing art and is dispensing with the need for human judgment. It is true that the introduction of instruments of precision into medicine has been of great service but the interpretation of the results obtained by them in the individual case still demands wisdom and experience on the part of the doctor. Where the machine is greater than the man the patient perishes. A large section of the public does not understand this. It has such an incorrigible love for apparatus,

and what it produces, that it hailed with acclamation a box of gadgets, constructed in defiance of all scientific principles, which claimed to hand out an exact diagnosis, and even the appropriate treatment, and thus make the application of so fallible a thing as the human mind unnecessary. Failing the reduction of medicine to machinery, the public seeks salvation in the specialist and the expert; and the more apparatus, and the more complicated, employed by these, the greater its confidence."—LORD HORDER. "The Clinician's Function in Medicine," *New York State J. Med.*, 36, 843 (June 1, 1936).—*Journal A. M. A.*

KILMER MEMORIAL.

A section of timberland in the Blue Ridge Mountains near the western tip of North Carolina will be dedicated on July 30th as the Joyce Kilmer Memorial Forest in honor of the soldier-poet of the 165th Infantry who was killed in the Battle of the Ourcq on that date in 1918.

The bronze tablet prepared for the dedication will bear the following inscription.

"Joyce Kilmer, 165th Infantry, Rainbow Division, soldier and poet, author of 'Trees,' born in New Brunswick, N. J., Dec. 6, 1886, killed in action in France, July 30, 1918.

"This memorial was initiated by the Bozeman Bulger Post, Veterans of Foreign Wars, and was selected by the United States Forest Service."

The poet was a son of our esteemed member, the late F. B. Kilmer.

WASHINGTON RESEARCH CENTER.

Dr. L. R. Thompson, Assistant Surgeon General of the Public Health Service, in charge of the scientific research division, announced the contemplated work at Bethesda, Md. Under the new establishment research activities will be carried on at Bethesda in conjunction with a training school for medical officers, classes for medical students, postgraduate courses for advanced physicians and public health officers, and an international information exchange which will attract public health leaders here from all over the world.

The Public Health Service, whose responsibilities and potentialities have been doubled by the Social Security Act, will have made a great stride forward when the Bethesda project is completed and functioning, Dr. Thompson believes. With Dr. Thomas Parran at the helm, the Public Health Service is in the midst of the most extensive program since its establishment.

LINDBERGH ARTIFICIAL HEART DEVICE.

Charles A. Lindbergh and Dr. Alexis Carrel will demonstrate their artificial heart apparatus to the scientific congress meeting in Copenhagen, August 10th. The Lindbergh pump, an artificial heart and lungs combined, permits such organs as spleens, hearts, kidneys, thyroids and ovaries to be revived and kept alive indefinitely. Previous attempts had resulted in only temporary success, because infection had cut short the after-life of the organs.

MENINGITIS VACCINE.

The boys in a CCC camp in Missouri served as test-tubes for the immunization against meningitis. Three hundred and ninety-five persons were vaccinated. Captain Kuhns, in reporting on the work in the *Journal of the American Medical Association*, cautions against too enthusiastic reception for the vaccine. This is only a preliminary report.

THE DROUGHT SECTION.

Many of our fellow members are suffering as a result of the drought, the locusts and other unfortunate conditions. Sympathy and encouragement can be expressed to them and hope that better things may come to them; these good people have endured their suffering with courage. Losses have come to the citizens of other sections from floods; the year seems to carry an unusual record of disasters.

Dr. Irvin Lavine, professor of chemical engineering at the University of North Dakota, has reported on the sodium sulphate deposits and Secretary M. O. Ryan of the State Planning Board is studying the economic problem. Wherever resources may be developed, it is hoped that the losses will in a measure be made up by successful ventures.

PROTAMINE INSULIN.

"The advantages of protamine insulin over ordinary insulin in the treatment of certain cases of diabetes were proclaimed by one of the co-discoverers of insulin, Prof. C. H. Best of the University of Toronto, at the meeting of the Canadian Medical Association, at Vancouver.

"The new kind of insulin was developed by Danish scientists. It was not intended to

supplant ordinary insulin in cases of diabetes which can be satisfactorily controlled by insulin alone, but was found a valuable adjunct to insulin in treating cases of severe diabetes. Protamine insulin is relatively insoluble and tends to be absorbed slowly and over a longer period of time than ordinary insulin. Consequently its blood sugar lowering effect lasts longer—twice as long, in fact.

"'The work of the Danish group on protamine insulin has been abundantly confirmed,'" Dr. Best said, "'Various groups of clinicians in Boston, Toronto, London and Rochester, Minn., have found that the duration of insulin action is much extended when insulin is combined under appropriate conditions with protamine.'"

"Dr. Best and his associate, Dr. Robert Kerr, found that dogs having no insulin-producing pancreas tissue could be kept free from symptoms of diabetes by one injection of protamine insulin daily. At least two injections of regular insulin are needed to accomplish this result. The fluctuations observed in the amount of sugar in the blood when regular insulin is used are avoided with protamine insulin."—*Science News Letter*, July 4, 1936.

SECTION N—MEDICAL SCIENCES, SECTION N_2—PHARMACY.*

The subsection on Pharmacy held one session on Thursday morning at which John C. Krantz, Jr. (University of Maryland) presided. Marvin R. Thompson (University of Maryland) reviewed the pharmacology of the alkaloids of ergot. He pointed out the differences between the new alkaloid of ergot which is now called ergonovine and other alkaloids of ergot of the ergotoxine-ergotamine group. He emphasized that the colorimetric reaction for the evaluation of ergot used in the British Pharmacopœia estimates all of the alkaloids whereas the new alkaloid, ergonovine, differs quite markedly pharmacologically from the alkaloids of the ergotoxine-ergotamine group.

H. B. Haag (Medical College of Virginia) discussed the assay of digitalis using the pigeon as the test object. The method did not employ the minimum emetic dose as was employed by Hanzlik and others but on the other hand he showed that the toxic dose is a trustworthy guide to the potency of digitalis when the pigeon is used as a test object.

Heber W. Youngken (Massachusetts College of Pharmacy) gave a detailed description of the pharmacognostic methods of differentiating between the anterior lobe of the pituitary body and the posterior lobe of the pituitary body as these substances appear on the drug market to be used for medication.

F. K. Riggs (Rutgers University) discussed the assay of Vitamin B_1 and pointed out that more specific methods than rat growth were necessary. He also emphasized that an absorbate of Vitamin B_1 on international clay was not as valuable as crude yeast and other products that contain B_1 in the restoration of rats that have been placed upon a Vitamin B_1 deficiency diet.

L. F. Tice (Philadelphia College of Pharmacy and Science) discussed the colloid chemistry of the two types of gelatin, the acid-treated type and the lime-treated type. He showed that their iso-electric points were different and that for all scientific work for which these gelatins were employed, particularly for the suspensions of the halides of silver, it was necessary to point out which gelatin had been employed.

Ruth Musser (University of Maryland) reported a study of the use of cyanides on the rat sarcoma antidoting the rat against 3 lethal doses of cyanide by the Chen antidote. It was shown that the antidote of sodium nitrite and sodium thiosulphate not only antidotes the rat but also protects the viability of the tumor.

C. Jelleff Carr (University of Maryland) reported his studies on the use of dextrose fragments as a sugar substitute in diabetes. Animal experiments indicated that this substance bids fair to be a useful substitute carbohydrate in the diabetic diet.

William F. Reindollar (Maryland State Department of Health) presented a paper explaining a new method used for the titration of iodide and iodine as they occur in common solution in many of the United States Pharmacopœia preparations.

E. I. Evans (University of Chicago) discussed the emetic doses of extract of ergot, ergotoxine and ergonovine. He showed that ergonovine produced no emesis clinically as does ergotoxine. The meeting was closed by a paper by Richard A. Deno (Medical College of Virginia) presenting an elaborate histological study of the involution of the mouse uterus.

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* Held at University of Rochester, June 18, 1936.

PERSONAL AND NEWS ITEMS.

Dr. Harrison E. Howe indicates that there is a shortage in science teachers. He states that the demand is for the best trained men and for the best qualified chemists.

Josiah K. Lilly is the founder of Foster Hall, and other Foster memorials, the last of which has been erected on the cathedral triangle, Pittsburgh University campus. This foundation enlarges the aims of Mr. Lilly. The inauguration of the annual "Foster Song Week" will be featured in the public and private schools, theatres and clubs of the nation. A fund is to be created which will be used solely for the benefit of needy musicians of unquestioned ability. The third promotion is a renaissance in singing of the American people.

Dean Charles F. Heebner, of Ontario College of Pharmacy, was honored by the presentation of an oil painting. Greetings were sent by pharmaceutical organizations and schools. Addresses were made by President H. J. Cody of the Univesity of Toronto, the Minister of Health, J. A. Faulkner, the graduates, alumni association and representatives of other bodies. Dean Heebner came to Ontario College of Pharmacy in 1891 and is a Life Member of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Gleb A. Popoff, student director of Drug Garden, AMERICAN PHARMACEUTICAL ASSOCIATION, University of California College of Pharmacy, San Francisco, has prepared a compilation of Plant Names with derivation and meaning of botanical names of medicinal plants. The purpose is assistance to the student of pharmacognosy; it has 52 pages, neatly manifolded. The arrangement is that of Youngken's "Text Book of Pharmacognosy" and some of the material is compiled from Kraemer, Culbreath, Trelease, Liddell-Scott and Andrews. The book is not for sale, it is compiled expressly for the pharmacognosy class of the University of California, College of Pharmacy, and maintains University form and reflects credit.

George H. P. Lichthardt, fellow member, is senior chemist for California State Highway Commission. He is a graduate in pharmacy; later, he took up the study of law and was admitted to the Bar.

Prof. Charles H. Rogers has been elected Dean of the College of Pharmacy of the University of Minnesota to succeed **Dr. Frederick J. Wulling,** who has retired after long years of service.

Dean A. G. DuMez has been appointed a member of the Committee of the International Pharmaceutical Federation. In addition other members of the Committee of the Federation include:

Dr. A. Chalmeta of the University of Madrid; W. van der Vorst, of the Nationale Pharmaceutique de Belgique; Dr. A. Schmierer, of the Deutsche Apothekerschaft; Dr. A. Jermstad, of the Norsk Pharmaceutisk, A. Ovon Kontsansky, of the Ungarische Apotherker-Verein; and Dr. T. Potjewidj, of Leyden, Belgium, *Secretary*.

James C. Munch presented a paper before American Association for the Advancement of Science in Rochester on the use of pancreas extract from which all insulin had been removed for the treatment of *Angina pectoris*. Five hundred cases had been treated successfully in 85 per cent of 500 cases, and in 400 cases of high blood pressure, with good results.

Frank L. Connors, prominent druggist of Montreal and *Second Vice-President* of the Quebec Pharmaceutical Association, has been appointed Minister without portfolio in the new Quebec Cabinet.

Rhode Island physicians here have expressed their appreciation of service provided by Providence and Cranston pharmacies whose stores are stations where physicians may leave specimens for examination. Coöperating drug stores are: E. P. Anthony, Blanding & Blanding, J. E. Breman & Co., First Aid Drug Store, Fleishman's Pharmacy, Gardner Drug Co., Haeseler Laboratory, Mason's Pharmacy, Professional Pharmacy and Walter R. Thorpe.

Dr. R. Bienfang, in reporting on positions secured by this year's graduates in pharmacy, declared that nine of the 1936 graduates have secured appointments as pharmacists in Oklahoma drug stores.

Dr. Joseph A. O'Hara, president of the Louisiana Department of Health, said no action would be taken for some time after August 1st for failure of manufacturers to register, "although we shall expect a response from the manufacturers whom we address on the subject." Dr. O'Hara said it probably would be about the first of January 1937 before his department could take any action against manufacturers for failing to comply.

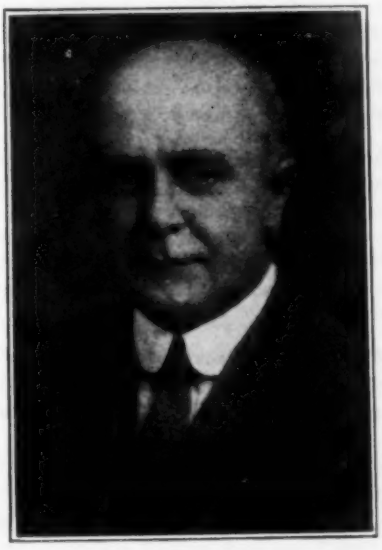
OBITUARY.

DEATH OF SIR HENRY S. WELLCOME.

It is with profound regret that we announce the demise of Sir Henry S. Wellcome in London on July 25th, aged 83 years. He was elected a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1875. The news of his death came too late for including a biographical sketch in this issue of the JOURNAL; in the meantime may we refer to the April JOURNAL for 1934, page 285, and to the succeeding issue, page 491. A distinguished citizen of the world and outstanding pharmacist has ceased his labors. A biography and tribute will appear in the August number of the JOURNAL.

W. BRUCE PHILIP.

Waldemar Bruce Philip, 80th president of the AMERICAN PHARMACEUTICAL ASSOCIATION, died in San Francisco July 13th, aged 58 years, following an illness during the greater part of a year. Several months ago Mr. and Mrs. Philip returned to California hoping to come back to Washington after the former's restoration to health. However, it was otherwise decreed and the members of the ASSOCIATION are saddened by the passing of one of their



W. BRUCE PHILIP.

associates, who was always ready to serve in the interests of pharmacy, and they sympathize with the widow and other members of the bereaved family.

As president, Mr. Philip presided at the Madison Meeting and shared with Chairman S. L. Hilton in the concluding ceremonies, on May 9, 1934, at the closing of the corner-stone of the AMERICAN INSTITUTE OF PHARMACY.

Waldemar Bruce Philip was born in Sacramento, Calif., July 19, 1878. His mother died when he was three years old and Bruce was placed in care of a friend of the family until, nine years later, his father remarried.

The youth attended the grammar and high schools of Sacramento and during part of this period Bruce had a carrier's route for the daily *Sacramento Record Union;* his contact with the family of Dr. C. A. Miller had instilled the desire to become a druggist and secure a college education. He engaged with O. P. Willis, and later with George Munroe at Fresno. The contact with the personnel of this pharmacy and its patrons influenced the ideals of the young man. He had saved enough money to begin his college studies and secured a position with Dr. Albert L. Stoll in San Francisco and matriculated at the San Francisco College of Pharmacy. He registered as pharmacist and returned to San Francisco, engaging with his former employer, O. P. Willis, now Willis and Martin, and after a year as employee he became a partner in the pharmacy.

In 1903, Mr. Philip entered for the "Doctor of Pharmacy" course in New York College of Pharmacy and, after conclusion of the work, returned to the Sacramento pharmacy. On November 24, 1904, he married Miss Fayetta Harris, a classmate at the California College of Pharmacy. February following, the firm of Philip and Philip established a pharmacy in Fruitvale; later, two branch stores were opened; these were disposed of but ownership of the buildings was retained. The Alameda County Association and San Francisco Retail Druggists' Association were organized at Mr. Philip's suggestion and these have functioned in the interests of the members and benefit of pharmacists in other sections of the State and country.

The Hastings College of Law, of the University of California, was organized in 1920. Mr. Philip matriculated and was admitted to the bar in 1923. He lectured and instructed in commercial pharmacy and pharmacy laws at the University for a decade. He was elected

Grand Regent of Kappa Psi Pharmaceutical Society and served in that capacity for a number of terms. *The Mask*, of April 1931, gave an interesting and comprehensive account of the services rendered in pharmaceutical organizations and for pharmacy; a sketch also appears in the JOURNAL A. PH. A. of January 1932. References are made to these activities as president of the Alameda County Pharmaceutical Association, as chairman of its legislative and executive committees, as secretary of the latter and also of the Retail Druggists of San Francisco; he suggested the students' loan funds of the latter. He is a former president of San Francisco Secretaries' Club, member of several alumni organizations. Philadelphia College of Pharmacy and Science honored him with the PH.M. degree and the National University, Washington, conferred on him the degree of Master of Law.

The deceased was a member of the Board of Trustees U. S. P. XI. He served as chairman of the House of Delegates, A. PH. A., vice-chairman of the Council, A. PH. A. and member of important committees.

He was vice-president of the National Association of Retail Druggists, member of important committees and for a number of years its Counsel and Washington representative. He published a *Bulletin* dealing with pharmaceutical legislation and other topics relating to pharmacy and the drug-trade activities.

The funeral ceremonies of the deceased were attended by representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION, the National Association of Retail Druggists, Veteran Druggists' Association, California State Pharmaceutical Association, Northern California Retail Druggists' Association, Southern California Retail Druggists' Association, Kappa Psi Fraternity, California College of Pharmacy, Attorneys' and Drug Clerks' Associations. Dr. Franklin T. Green and John Culley were pall-bearers.

JOHN URI LLOYD MEMORIAL ISSUE.

The *Eclectic Medical Journal* for May is a memorial issue. The first article is that of the publication—a comprehensive biographical sketch; other tributes have been selected. The biographical sketches include the following: "A Character Sketch," by Adolph G. Vogeler; "John Uri Lloyd, Pharmacal Pathfinder," by Russel Manning; "Ohio Eclectics Honor John Uri Lloyd," "Introduction Remarks," by Byron H. Nellans, M.D.; "John Uri Lloyd—the Author," by William P. Best, M.D.; "John Uri Lloyd as a Pharmacist," by the late Caswell A. Mayo; "John Uri Lloyd—the Teacher," by Rollo L. Thomas, M.D.; "American Contemporaries—John Uri Lloyd," by Martin H. Fischer, M.D.; "We Spend the Day with Lloyd," by Felix J. Koch; "John Uri Lloyd—Rebel," by Murray Breese; "John Uri Lloyd as a Pharmacist," by James H. Beal; "John Uri Lloyd," by Ivor Griffith; "John Uri Lloyd—Teacher, Man, Friend," by William Nelson Mundy, M.D.; "John Uri Lloyd—An Inspiration," by C. S. Amidon, M.D.; "John Uri Lloyd," *Cincinnati Post*. "Memorial Services for Lloyd in Japan." "The Departure of a Gentle Spirit." "Memorial Resolution," by the Board of Trustees of the Eclectic Medical College." "John Uri Lloyd, Noted Cincinnatian, Dies," *Cincinnati Times Star*.

A. W. POOLE.

A. W. Poole, pharmacist at Clarendon, Va., died July 9th, aged 61 years. After graduation from George Washington University in 1900, Mr. Poole entered the drug business in Georgetown, where he remained for 33 years. Three years ago he moved his business to Arlington County, where he made his home.

Arthur Amos Noyes, former Director of the Gas Chemical Laboratory, at the California Institute of Technology, died June 3rd. Dr. Noyes received the Willard Gibbs Medal in 1927 and the Davy Medal in 1932. He was president of the American Chemical Society in 1904.

Mrs. Leslie V. Caspari, widow of the late Professor Charles Caspari, died July 16th, aged 83 years. Members and all other pharmacists will remember the late Charles Caspari, who was active for many years in the ASSOCIATION. Mrs. Caspari was the mother of Dr. Charles E. Caspari, Dean of the St. Louis College of Pharmacy.

ANNUAL REPORT ON TRAFFIC IN NARCOTICS.

According to the report of the Commissioner of the Bureau of Narcotics, $244,899,000 was appropriated for the enforcement of the Federal Narcotic Laws for the fiscal year 1935. A uniform narcotic law has been approved by the National Conference of Commissioners of Uniform State Laws.

SOCIETIES AND COLLEGES.

OFFICERS-ELECT, AMERICAN PHARMACEUTICAL ASSOCIATION FOR 1936–1937.

President-Elect, George D. Beal, Pittsburgh, Pa.

First Vice-President Elect, J. Leon Lascoff, New York, N. Y.

Second Vice-President Elect, James C. Munch, Lansdowne, Pa.

Members Elect of the Council: H. C. Christensen, Chicago, Ill.; R. P. Fischelis, Trenton, N. J.; Ernest Little, Newark, N. J.

These officers will be installed at the annual meeting of the ASSOCIATION in Dallas, Texas.

NORTH PACIFIC BRANCH, A. PH. A.

Immediately following reports by Dean A. Ziefle, secretary of the O. S. P. A. educational fund, and Dean A. O. Mickelsen, chairman of the Pharmacy Week committee, the North Pacific Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION will present the following program under the direction of President Fred Geue: "Changes and Revision of U. S. P. and N. F.," by Professor E. T. Stuhr of Oregon State College; "White Mineral Oil and Petrolatum in Pharmacy," by Dean A. O. Mickelsen of North Pacific College, followed by comments on mineral oil by L. B. Benjamin.

AMERICAN CHEMICAL SOCIETY ANNIVERSARY.

The sixtieth anniversary of the American Chemical Society will be celebrated at a 5-day national meeting in Pittsburgh, beginning September 7th.

SOCIETY FOR THE HISTORY OF PHARMACY.

The meeting of the Society for the History of Pharmacy was held in Stuttgart, Germany, June 16th to 18th; this also represents the 10th anniversary of the organization.

Dr. Häfliger, the president of the organization, presided. In his address he referred to the activities of the Association during the ten years and the results which followed. He complimented the work of Dr. Fritz Ferchl.

Dr. O. Zeckart referred to the work of Karl Wilhelm Scheele. Dr. George Edmund Dann delivered an address in which he gave a comprehensive genealogy of the apothecary and chemist, Martin Heinrich Klaproth. It is interesting to note that two members of the family, namely the one referred to, and Julius Klaproth, were outstanding in their respective fields—the former as chemist and the latter as orientalist.

SAM P. HARBEN.
Chairman, Texas Post-Convention Tours.

AMERICAN PHARMACEUTICAL ASSOCIATION meets in Dallas, August 24th–29th.

TAMPA HEALTH COUNCIL.

E. P. Purcell, president of the Hillsborough County Retail Druggists' Association, was elected *President* of the newly organized Hillsborough County Allied Health Council, comprising a membership of doctors, dentists, nurses and druggists. Other officers elected were: Dr. T. Rector, *First Vice-President;* Dr. C. J. Caraballo, *Second Vice-President;* Mrs. Maud Darlington, *Secretary and Treasurer.*

ILLINOIS FAIR TRADE ACT.

The Illinois Supreme Court has handed down a decision upholding the constitutionality of the Illinois Fair Trade Act in the case of Triner *vs.* McNeil. Quoting *C. R. D. A. News:* "Fair Trade Legislation resting as it does upon a sound, equitable commercial and legal foundation, namely, that one or a small group cannot so conduct themselves as to injure a great majority, must in the course of human progress adjust itself so that its benefits will be for the greater good of the greatest number."

BRITISH PHARMACEUTICAL CONFERENCE.

The 73rd annual meeting of the British Pharmaceutical Conference was held at Bournemouth during the week of June 23rd. The annual address was presented by Chairman Harold Deane. Twenty-two conference papers were presented and discussed, dealing with pharmaceutical subjects relating to British pharmacy.

CONNECTICUT BOARD OF PHARMACY.

William J. Dunphy succeeds Edward J. Murphy as president of the Connecticut Board of Pharmacy Commissioners and Hugh P. Beirne was reëlected secretary-treasurer. Other members are George Blackall and Edward J. Murphy.

DELAWARE PHARMACEUTICAL SOCIETY.

The fiftieth annual meeting of the Delaware Pharmaceutical Society was held at the Hotel Belhaven, Rehoboth Beach, June 29th and 30th. Dr. Marvin J. Andrews, professor of pharmacy of The School of Pharmacy, University of Maryland, spoke on "U. S. P. and N. F. Propaganda to the Physician," with special reference to the new admissions. Dr. Robert L. Swain spoke on "Fair Trade Laws in General and Operation of Pharmacy Law in Maryland." Thomas Donaldson, chairman of Legislative Committee, gave an historical sketch of Delaware Pharmaceutical Society.

Motion passed that a letter of thanks be sent Secretary E. F. Kelly of the AMERICAN PHARMACEUTICAL ASSOCIATION for his untiring efforts and splendid work in helping the pharmacist to become recognized in the U. S. Army.

The following officers were elected: *President*, Edward J. Elliott, Bridgeville; *First Vice-President*, Frank E. Brereton, Milford; *Second Vice-President*, Peter Paul Potocki, Wilmington; *Third Vice-President*, William Earl Hastings, Selbyville; *Treasurer*, Albert Dougherty, Wilmington; *Secretary*, Albert Bunin, Wilmington.

KENTUCKY ASSOCIATION.

The following were elected officers of Kentucky Pharmaceutical Association: *President*, Morris D. Spoonamore, Danville; *Vice-Presidents*, C. E. Montgomery, Owensboro; Emil Nehring, Covington; Oscar Votteler, Louisville; *Secretaries*, J. W. Gayle, Frankfort, and H. J. Hafendorfer, Louisville; *Treasurer*, William J. Johnson, Mayfield; *Board of Directors*, Harry Frankel, Louisville; W. H. Poynter, London; and W. H. Fisher, Louisville.

MARYLAND ASSOCIATION.

Harry W. Matheny, retiring president of Maryland Pharmaceutical Association, recommended the appointment of a coöperative pharmacy planning committee of the Board of Pharmacy and School of Pharmacy.

Melville Strasburger, Baltimore, was elected *President*. Other officers for the ensuing year are: A. A. M. Dewing, Centreville, *First Vice-President;* A. N. Hewing, Baltimore, *Second Vice-President;* Lloyd Richardson, Bel Air, *Third Vice-President;* Harry S. Harrison, Baltimore, *Treasurer;* Robert L. Swain, reelected *Editor, The Maryland Pharmacist;* E. F. Kelly, Baltimore, reëlected *Secretary*. J. W. Westcott, Baltimore, was elected *Honorary President*.

MARYLAND ASSOCIATION RESOLUTIONS.

Resolved, that the Association express its profound gratitude to the AMERICAN PHARMACEUTICAL ASSOCIATION, and particularly to its tireless secretary, Dr. E. F. Kelly, for having waged a successful fight for the recognition of pharmacy as a profession in the government services, and for having federal legislation enacted providing for commissions for pharmacists in the United States Army, and be it

Further resolved, that we express our confidence in the purposes and ideals of the AMERICAN PHARMACEUTICAL ASSOCIATION, and pledge our best efforts in behalf of the wide range of activities which the ASSOCIATION carries on.

MASSACHUSETTS ASSOCIATION.

The following officers were elected by Massachusetts Pharmaceutical Association: *President*, Harry S. Bernstein, Springfield; *First Vice-President*, James L. Case, East Boston; *Second Vice-President*, John J. Morrissey, Lawrence; *Treasurer*, Lyman W. Griffin, Boston; *Secretary*, Carl G. A. Harring, 20 Glen Road, Newton Center. C. Herbert Packard and James F. Finneran were elected to the *Board of Trustees*.

NEW JERSEY ASSOCIATION.

New Jersey Pharmaceutical Association elected the following officers: *President*, Charles R. Garrabrant, Passaic; *First Vice-*

President, Emil P. Martini, Hackensack; *Second Vice-President*, Jerome Kahn, Caldwell; *Secretary*, Prescott R. Loveland, Trenton; *Treasurer*, Charles J. McCloskey, Branchville. *Committee on Public Health and Welfare* (for three-year terms): Carl H. K. Ruopp, Trenton; Edward C. White, Hoboken.

The New Jersey Board of Pharmacy presented Secretary R. P. Fischelis with a beautifully engrossed and illuminated set of resolutions in recognition of his ten years of service as secretary of the Board of Pharmacy.

NEW JERSEY BOARD OF PHARMACY.

Charles Schamach succeeds C. Graham McCloskey as member of the New Jersey Board. The officers of the Board are: *President*, Dean B. Crawford; *Vice-President*, James A. Bauman; *Treasurer*, Albert J. Smith; *Secretary*, Robert P. Fischelis.

NEW YORK STATE PHARMACEUTICAL ASSOCIATION.

The 58th annual meeting of New York Pharmaceutical Association was held June 16–19, 1936, at Bolton Landing, Lake George, N. Y.

Secretary Lehman reported an increase of 1517 members since last convention, making the total enrollment 6441, divided into 6321 active members, 113 life, 7 honorary. Twenty-one members died during the year. The treasurer reported a balance of $14,000.00.

Secretary of the New York State Board of Pharmacy, George W. Mather, reported that although quite a number of new graduates had been registered during the past fiscal year, the number of licenses issued and renewed was practically the same as last year, showing that many had died or retired from business during that period.

He recommended that legislation be inaugurated which will oblige the manufacturers of proprietary and secret remedies to reveal the therapeutic or active ingredients of their preparations, so as to facilitate the control of the sale of poisonous, deleterious and/or habit-forming drugs under the Dunckel Law.

Among the resolutions approved were: the one providing for a mid-winter meeting; also one asking the pharmacy law amendment so as to require a year of additional practice after graduation; one inviting the AMERICAN PHARMACEUTICAL ASSOCIATION to hold its 1937 meeting in New York City; one increasing the Executive Committee to five or seven members; requiring the registration of manufacturers of pharmaceutical products, containing poisonous, deleterious and habit-forming ingredients; reaffiliation with the N. A. R. D.

The following officers were elected: *President*, Morris Brodkin, Bronx, New York City; *First Vice-President*, Edgar S. Bellis, Bronxville; *Second Vice-President*, Percy Goldman, Brooklyn; *Third Vice-President*, Thos. A. J. Rocchio, Bronx, New York City; *Secretary*, Robert S. Lehman, Brooklyn; *Treasurer*, Richard A. Austin, Cairo; *Chairman, Executive Committee*, Fred. C. A. Schaefer, Brooklyn; *Honorary President*, Frederick D. Ostrander, Gloversville; *Honorary Life Member*, Dr. Willis G. Gregory, Buffalo.

Twelve very interesting papers on scientific subjects were read.

NORTH CAROLINA ASSOCIATION.

P. J. Suttlemyre, of Hickory, has been elected president of the North Carolina Pharmaceutical Association. Others elected were: C. C. Fordham, Jr., Greensboro, *First Vice-President;* John C. Brantley, Jr., Raleigh, *Second Vice-President;* Joseph Hollingsworth, Mount Airy, *Third Vice-President;* John Beard, Chapel Hill, reëlected *Secretary-Treasurer.*

NORTH DAKOTA ASSOCIATION.

The following officers were elected by North Dakota Pharmaceutical Association: *President*, Andrew E. Erickson, Fargo; *Vice-Presidents*, Philip Boise and Harry Gray; *Treasurer*, P. H. Costello; *Secretary*, Dean W. F. Sudro.

RHODE ISLAND ASSOCIATION.

Dr. Edward A. McLaughlin, director of the state department of public health, in his address before Rhode Island Pharmaceutical Association said that a program of greater coöperation between physicians and pharmacists would result in the writing of more prescriptions. Rhode Island Association convened at Watch Hill.

TEXAS ASSOCIATION.

Immediately following the closing session of the Texas Pharmaceutical Association in San Antonio, the executive committee held a meeting. At this time, L. D. Gilmore of San Antonio, succeeding Henry Hein of San Antonio, whose term expired, was elected *Vice-Chairman* of the executive committee.

The meeting was attended by B. B. Brown, Dallas, *President;* Festus Pierce, Corsicana,

First Vice-President; W. U. Paul, El Paso, *Second Vice-President;* L. D. Gilmore, San Antonio, *Vice-Chairman;* A. G. Heinrichs, Houston, new member succeeding E. B. Oliver of Longview; Roy Pool, Amarillo; Murray Thames, Beaumont; J. C. Frazier, Fort Worth; Shine Philips, Big Spring. W. J. Danforth of Fort Worth was elected *Secretary-Treasurer;* he was given a vote of thanks and confidence and was instructed to continue the legislative policies of the past year.

President Brown appointed a committee to consider the recommendations included in the president's address. A plan for emblems for association members and a prestige program to build up public confidence in qualified ethical pharmacists was included in the survey of the possibilities. The tentative radio plan includes a fifty-two week contract with a thirty-minute program weekly containing music, educational script and guest speakers from scientific professions. Dental, medical and pharmaceutical addresses are planned.

The committee instructed Secretary Danforth to issue the association bulletin semi-monthly or as often as necessary during the legislative sessions. The bulletin is a mimeographed sheet containing important news of association affairs. It is sent to all members. He was also instructed to proceed with the formation of a Southwestern Conference of Pharmaceutical Associations, which has been proposed. This organization, a non-profit, non-dues association will meet annually with representatives, probably the president and secretary, of each state association in the five states of the Southwest, to discuss matters of mutual interest, to plan methods of supporting fair trade, profit stabilized products. Matters of conflicting convention dates and other details will also be cared for by this group.

VERMONT ASSOCIATION.

Vermont Pharmaceutical Association elected the following officers: *President,* Joseph W. Blakeley, Montpelier; *Vice-President,* Fred W. Wheeler, Springfield; *Second Vice-President,* Albert E. Cox, Hardwick; *Third Vice-President,* Fred Beauchamp, Rutland; *Secretary-Treasurer,* Lester C. Chickering, Brattleboro.

VIRGINIA ASSOCIATION.

President E. P. Berlin, of Virginia Pharmaceutical Association, recommended a continuation of the organization of a legislative program. He referred to the successes of the past year and in particular to the enactment of Virginia's fair trade law. The association held its annual session on board the *S. S. Reliance,* en route to Bermuda.

WASHINGTON STATE ASSOCIATION.

The following were elected officers of Washington Pharmaceutical Association: *President,* Michael J. Grady, Colfax; *Vice-President,* Roy Millett, Yakima; *Treasurer,* W. H. Hinman, Seattle; *Secretary,* M. P. Goodner, Seattle.

WISCONSIN PHARMACEUTICAL ASSOCIATION.

The retiring president, John F. Huber, advocated legislation restricting the sale of drugs to registered pharmacies, and an anti-peddling bill. A feature of the convention was the pharmaceutical clinic conducted by faculty members of the course in Pharmacy of the University of Wisconsin, which was followed by a professional open forum.

A certificate of merit for outstanding work in pharmacy in Wisconsin was awarded to Herman L. Emmerich, Milwaukee, and Charles Charmley was given the Pharmacy Week Cup. The following officers were elected: *President,* A. A. Krygier, Milwaukee; *Vice-President,* Karl J. Henrich, Superior; *Second Vice-President,* Otis George, Sparta; *Third Vice-President,* William Hoeschler, La Crosse; *Treasurer,* B. F. Leidel, Milwaukee; *Secretary,* Jennings Murphy, Milwaukee.

WYOMING ASSOCIATION.

Wyoming Pharmaceutical Association elected the following officers: *President,* H. H. Cordiner of Laramie; *First Vice-President,* Ira J. Burleson, Riverton; *Second Vice-President,* Frank Korfanta, Rock Springs; *Secretary-Treasurer,* John B. Tripeny, Casper. *Place of Meeting,* Casper. *Time,* 1937.

The association has gone on record as favoring the enaction of a Fair Trade Law and a law relating to the sale, control and licensing of sanitary or prophylactic products for the prevention of venereal and other diseases and infections.

OFFICERS OF STATE ASSOCIATIONS.

Arkansas.—*President,* Harold W. Lawson, Little Rock; *First Vice-President,* William Griffin, Heber Springs; *Second Vice-President,* A. L. Davis, Texarkana; *Secretary-Manager,* W. Irl Brite, Ben McGehee Hotel, Little Rock; *Treasurer,* Troy Churchman, N. Little Rock.

Colorado.—*President*, Clyde C. Phillips, Jr., Colorado Springs; *First Vice-President*, H. Rodney Anderson, Montrose; *Second Vice-President*, Ralph E. Kemp, Lafayette; *Treasurer*, V. N. Lagerquist, La Junta; *Secretary*, Charles J. Clayton, Denver.

Georgia.—*President*, Hoke S. Peters, Manchester; *First Vice-President*, J. W. Brinson, Wrightsville; *Second Vice-President*, W. W. Fincher, Canton; *Third Vice-President*, Bonnie Brown, Lyons; *Secretary*, Z. O. Moore.

Indiana.—*President*, A. J. Dougherty, South Bend; *Secretary*, F. V. McCullough, New Albany; *Vice-Presidents*, Ralph Thornburg, Syracuse, and C. E. Reed, Winchester.

Maine.—*President*, H. W. Ormsby, Houlton; *First Vice-President*, P. S. Demers, Springvale; *Second Vice-President*, Carl Anderson, Bath; *Third Vice-President*, Frank Hargraves, Mexico; *Secretary*, J. H. Allen, Waterville; *Treasurer*, George O. Tuttle, Portland.

Oklahoma.—*President*, Jesse W. Stunkle, Enid; *First Vice-President*, B. M. Jones, Tulsa; *Second Vice-President*, Dave McLemore, Britton; *Secretary*, Elbert Weaver, Stillwater; *Treasurer*, G. C. Cooper, Edmond.

Oregon.—*President*, M. C. Kaegi, Portland; *Vice-President*, A. S. Keir, Hood River; *Secretary*, Lawrence Stovall, Portland; *Treasurer*, E. A. Bachman, Portland; *Assistant Secretary and Manager*, J. J. Lynch, Portland.

(*To be continued.*)

INVITATION.

Members of the American Pharmaceutical Association:

"Texas awaits you, Dallas will warmly welcome you and we hope you will immediately arrange your business and social affairs so as to enable you to attend the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION to be held in Dallas, Texas, August 24th–29th. Your officials are arranging a valuable program for all sections.

"In addition to all of these things arranged for you in Dallas, which include two full days of sight-seeing at the Texas Centennial Exposition, a big world show, the greatest birthday party ever given.

A post-convention tour has been contracted for, probably the most economical visit ever arranged for a visit to a foreign country.

"See romantic, historic, ancient and scenic Old Mexico. When you cross the Rio Grande River into Old Mexico at Laredo, you immediately pass back into the sixteenth century. You have never enjoyed a post-convention tour as you will this one."

If you have not done so—write the Local Secretary, who closes his invitation and message:

"We want you in Texas, we want you in Dallas, we want you to bring the wife along; make a family party of this meeting, include business with pleasure, attend your favorite convention and have a wonderful vacation and sight-seeing trip, all in *One*."

W. D. ADAMS, *Local Secretary*.

PARTIAL TENTATIVE PROGRAMS FOR THE DALLAS MEETING.

Not all of the programs of the Convention are published, but will be part of the Official Program. Some programs have been published and will *not* be repeated at this time. The Tentative Program of the American Association of Colleges of Pharmacy was printed in the May JOURNAL, pages 454–455.

The program of the Conference of Teachers of Pharmacognosy and Pharmacology was printed in the June issue of the JOURNAL, page 567.

The program of National Conference of Pharmaceutical Research was printed in the May JOURNAL, pages 456–457.

The program of the Plant Science Seminar was printed in the June JOURNAL, pages 567–568.

The General Program for the Annual Meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION and affiliated organizations, is printed in this issue of the JOURNAL, pages 644–646.

Other programs, as far as completed, follow. The **Scientific Section** so far has listed 68 papers and will be assigned in the Official Program.

PROGRAM, SECTION ON EDUCATION AND LEGISLATION.

1. Remarks by Chairman C. Leonard O'Connell.
2. Remarks by Vice-Chairman George C. Schicks.
3. Report of Secretary George A. Moulton.
4. Reports of Standing Committees. Appointment of New Committees. Resolutions and Nomination.
5. Address: "Observations on Legislation," Roy B. Cook.
6. Paper: "Pharmacy's Position under Regulated Community Medicine," P. J. Callaghan.
7. Address: "Legislative Requirements for the Future," W. Mac Childs.
8. Paper: "A Novel Pharmaceutical Organization," Oscar Loddy.
9. Paper: "Foundations for Successful Legislation," George A. Moulton.
10. Paper: "The Robinson-Patman Bill," Paul C. Olsen.
11. Paper: "Requirements for Entrance to the Pharmacy Course," H. C. Christensen.
12. Paper: "Legislative Weather Vanes," Robert L. Swain.
13. Paper: "Professional Pharmacy in National Legislation," E. F. Kelly.
14. Paper: "Some Important Obligations and Responsibilities of a College of Pharmacy," Ernest Little.
15. Paper: "An Adventure in Pharmaceutical Curriculum Construction," H. C. Newton.
16. Paper: "High School Grades and State Board Results," H. Evert Kendig.
17. Address: "Legislation and Politics." Speakers to be announced.
18. "Should High School Graduates Alone Be the Basis for College Entrants?" Robert W. Rodman.
19. "The Next Step," W. T. Rudd.
20. Reports of Appointed Committees.
21. Election of Section Officers.
22. New Business and Adjournment.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

1. "Is Dispensing and Preparation of Medicinal Substances a Lost Art?" Max N. Lemberger.
2. "Sterile Fluids for the Hospital and the Pharmacist," Evelyn Gray Scott.
3. "Pharmacist and Physician," Ella Paquin.
4. "Mal Practice of Pharmacy," E. J. Parr.
5. "The Teaching of Manufacturing Pharmacy," H. G. DeKay.
6. "Correct Prescription Pricing," George L. Secord.
7. "The Study of Glycerin Suppositories," William A. Prout.
8. "A Comparative Study of the Antiseptic Properties of Certain Ointments Employing Various Bases," William A. Prout and Mae Strickland.
9. "A Uniform Schedule for Prescription Pricing in South Dakota," Clark T. Eidsmoe.
10. "Subject to be Announced," Mac Childs.
11. "Pharmacy in Prison," Charles L. Pickens.
12. "The Establishment and Operation of an Open-All-Night Policy in a Retail Pharmacy," Herman and Robert Elich.
13. "The Clinic Pharmacy," Josephine Nichols.
14. "Pharmacy from the Standpoint of Hospital Administration," B. T. Howiler.
15. "Practical Medical Economics," Frank B. Kirby.
16. "The Color of Morphine Sulphate," J. M. Ort and W. G. Christiansen.
17. "The Assay of Cysteine Hydrochloride," C. F. Bickford and R. E. Schoetzow.
18. "The Determination of Phenolphthalein in Mineral Oil Emulsions," C. F. Bickford and R. E. Schoetzow.
19. "Fluidextract Celery Fruit N. F. VI," P. L. Burrin and F. E. Bibbins.
20. "Mal-Practice of Pharmacy," E. J. Parr.
21. "A Study of the Cost of Sampling," L. W. Rising and Einar Nygren.
22. "Control of Specialties and Nostrums in Prescription Stock," John F. McClosky.
23. "A Preliminary Study of Tincture of Cantharides," Leslie M. Ohmart.
24. "The Challenge of Today," Anton Hogstad, Jr.
25. "A Greater Knowledge of Pharmacology Is Essential to a Professional Pharmacist," A. O. Mickelsen.
26. "The Inter-Allied Association in South Dakota," Kenneth Jones.
27. "One Year of U. S. P. and N. F. Extension in Mississippi," Charles E. Wilson.
28. "The Education of a Pharmacist," Ernst T. Stuhr.
29. "New Practicalities in Pharmacy," O. U. Sisson.
30. "The Idealism of Pharmacy," Sister M. Constance.

31. "Adapting Modern Business to Our Code of Ethics," Frank Coniglio.

SECTION ON HISTORICAL PHARMACY.

Chairman's Address.
Secretary's Report.
Report of Historian.
Appointment of Nomination Committee (Place at end of first session).

PAPERS.

1. "Is There Anything New under the Sun?" Theodore J. Bradley.
2. "Doctor Charles Rice," John Uri Lloyd—to be presented by J. T. Lloyd.
3. "Some Herb Remedies of the Aztecs," Emily Walcott Emmart.
4. "Three 17th Century New England Pharmacists," W. T. Bradley.
5. "An Interesting Old Medicine Chest," Charles Whitebread.
6. "Verbena in Early Roman Rites," C. J. Zufall.
7. "Jons Jacob Berzelius," Louis H. Roddis.
8. "A History of the Oklahoma State Board of Pharmacy," William G. Bray.
9. "A History of the University of Oklahoma School of Pharmacy," William G. Bray.
10. "A History of Oklahoma State Pharmaceutical Association," Wm. G. Bray.
11. "What Difference Does a Century Make?" John E. Kramer.
12. "J. Meyenberg, Drugs," Margaret Cousins.
13. "Reverchon, Texas Botanist," Margaret Cousins.
14. "Knowing the History of One's Profession, II," C. O. Lee.
15. "The Literary Pharmacopœia of Scott," Edward Kremers.
16. "Chuck Wagon Therapy," Walter Cousins.
17. "A Memorial Hour," contributors—James H. Beal and others. H. V. Arny in charge. Time to be selected.

PROGRAM, SESSIONS OF THE A. PH. A. HOUSE OF DELEGATES, DALLAS, TEXAS.

First Session, Tuesday, August 25, 1936, 1:30 P.M.

1. Call to Order.
2. Roll Call of Delegates.
3. Reception of Fraternal Delegates.
4. Opening Remarks by the Chairman, Roy B. Cook.
5. Appointment of Committee on Nominations.
6. Appointment of Committee on Resolutions.
7. Annual Report of the Council, E. F. Kelly, *Secretary*.
8. Report of the Treasurer, C. W. Holton.
9. Report of the Secretary, E. F. Kelly.
10. Reports of Delegates to Other Organizations (including International Pharmaceutical Federation, American Association for the Advancement of Science and National Drug Trade Conference).
11. Receipt of Resolutions, Reports and Other Communications, all of which must be in writing.
12. New Business.

Second Session, Wednesday, August 26, 1936, 8:00 P.M.

1. Roll Call of Delegates.
2. Reading and Adoption of the Minutes of the First Session.
3. Receipt of the Address of the President of the AMERICAN PHARMACEUTICAL ASSOCIATION.
4. Receipt of Reports and Other Communications from the Association, Council and Sections.
5. Receipt of Resolutions, Reports and Other Communications, all of which must be in writing.
6. Reports of the Committees on Cosmetics, H. C. Muldoon; on Pharmacy Week, Anton Hogstad, Jr., on Council on Pharmaceutical Practice, E. F. Cook; to Study the By-Laws, R. L. Swain; on Pharmacy Corps in the U. S. Army, H. E. Kendig; on Prescription Tolerances, H. H. Schaefer; on Development of Pharmacy Laws and Restrictive Legislation, R. L. Swain; on Professional Relations, L. A. Seltzer; on A. PH. A. Branches, Adolph Ziefle; on Legislation, E. F. Kelly; on Membership, E. F. Kelly.
7. Election of the Honorary President, Secretary and Treasurer of the ASSOCIATION upon nomination by the Council.
8. Report of the Committee on Nominations.
9. Report of the Committee on Place of Meeting.

10. Report of the Committee on Resolutions.
11. Unfinished Business.

Third Session, Friday, August 28, 1936, 2:00 P.M.

1. Roll Call of Delegates.
2. Reading and Adoption of the Minutes of the Second Session.
3. Receipt of Reports and other Communications from the ASSOCIATION, Council and Sections.
4. Reports of the Committees on Weights and Measures, M. N. Ford; on Study of Pharmacy, R. P. Fischelis; on U. S. Pharmacopœia, C. C. Glover; on Pharmaceutical Syllabus, J. C. Beard; on Horticultural Nomenclature, H. W. Youngken; on Physiological Testing, J. C. Munch; on William Procter, Jr., Memorial Fund, J. E. Hancock; on International Pharmaceutical Nomenclature, A. G. DuMez; on Press Relations, R. W. Rodman; on Prerequisite Legislation, C. B. Jordan; on Endowment Fund, Wm. B. Day; to Study Courses in the History of Pharmacy, C. O. Lee; on Professional Information Pertaining to Dental Pharmacy, Geo. C. Schicks; on Transportation, T. J. Bradley.
5. Final Report of Committee on Resolutions.
6. Unfinished Business.
7. Installation of the Chairman and Vice-Chairman of the House of Delegates.
8. Final Adjournment.

PROGRAM CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS.

First Session, Monday, August 24, 1936, 9:00 P.M.; Second Session, Thursday, August 27, 1936, 9:00 A.M.

1. Call to Order.
2. Remarks by Chairman, Robert L. Swain.
3. Report of Secretary, M. N. Ford.
4. Report of Finance Committee.
5. Appointment of Conference Committees.
6. Pharmacy Law Enforcement in the Following States:
   Texas—Walter H. Cousins
   Kansas—Pat Mulligan
   Mississippi—T. C. McMillion
   Arkansas—W. H. Parker
   Alabama—Samuel A. Williams
   Arizona—L. Evans, Jr.
   New Mexico—George Sasser
   Louisiana—John E. Guess
   Oklahoma—Edward Milligan
   Minnesota—Edward J. Prochaska
   (Mr. Prochaska will lay special emphasis on law enforcement and mail order houses.)
7. The Administration of the Minimum Equipment Law in:
   New Jersey—Robert P. Fischelis
   New York—George W. Mather
   Virginia—A. L. I. Winne
   Kansas—Mac Childs
   Maryland—Robert L. Swain.
8. The Sale of Drugs and Medicines in New York State, George W. Mather, Secretary, New York Board of Pharmacy.
9. Have Boards of Pharmacy Discretionary Powers in the Matter of Granting Permits for the Operation of Retail Pharmacies? Kenneth Jones, South Dakota.
10. Discussion of Legislation Affecting the Control of Pharmacies, Pharmacists and the Manufacture and Distribution of Drugs and Medicines, and Other Topics of Special Interest to Enforcement Officials.
11. Discussion of the Powers of Inspection Vested in Boards of Pharmacy.
12. A Discussion of the Advisability of Setting a Standard for Drug Stores in Which Practical Experience May Be Obtained —New York—George W. Mather, New Jersey—Robert P. Fischelis.
13. What Can Be Done to Regulate the Sale of Proprietary Medicines?—Hugo H. Schaefer.
14. What Can Be Done to Prevent Drugs and Medicines from Being Marketed under Fictitious Firm Names?—West Virginia —Roy B. Cook.

TENTATIVE PROGRAM N. A. B. P. CONVENTION.

First Session, Monday, August 24, 9:30 A.M.—Ball Room.

1. Call to Order, President Mac Childs.
2. Roll Call.
3. Appointment of Committee on Credentials, President Mac Childs.
4. President's Address, Mac Childs.
5. Appointment Committee on President's Address.
6. Report of Secretary, H. C. Christensen.
7. Report of Treasurer, J. W. Gayle.
8. Appointment of Nominating Committee, President Childs.
9. Report of Executive Committee, Clare Allan, *Chairman*.

10. Presentation of Suggested Amendments to Constitution and By-Laws, Walter Varnum.

Second Session, Monday, August 24, 1:30 P.M.—Ball Room.

1. Report of Advisory Examination Committee, H. C. Christensen, *Chairman*.
2. Report of Syllabus Committee.
3. Report of Legislation Committee, G. A. Moulton, *Chairman*.
4. Report of Committee on National Legislation, Robert L. Swain, *Chairman*.
5. Report of Committee on Prerequisite Legislation, C. W. King, *Chairman*.
6. Report of Publicity Committee, Hugh P. Beirne, *Chairman*.
7. Report of Grievance Committee, M. N. Ford, *Chairman*.
8. Report of Committee on National Certificate, H. C. Christensen, *Chairman*.
9. Report of Committee on Minimum Standards of Technical Equipment, A. C. Taylor, *Chairman*.
10. Report of Committee on Pharmaceutical Jurisprudence, Roy B. Cook, *Chairman*.
11. Report of Committee on Code Matters, Robert L. Swain, *Chairman*.
12. Report of Banquet Committee, Walter H. Cousins, *Chairman*.

N. A. B. P. Banquet, Monday, August 24, 6:30 P.M.—Palm Garden.

JOINT SESSION WITH AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY.

Tuesday, August 25, 9:00 A.M.—Ball Room.

Program not ready yet—details later.

Final Session, Tuesday, August 25, 1:30 P.M.—Ball Room.

1. Reports of Vice-Presidents:

   District No. 1, Vice-President George A. Moulton.
   District No. 2, Vice-President John M. Woodside.
   District No. 4, Vice-President Earl Durham.
   District No. 6, Vice-President Emmett Weaver.
   District No. 7, Vice-President R. C. Shultz.
2. Report of Committee on President's Address.
3. Report of Department of Education, R. L. Swain, *Director*.
4. Report of Committee on Constitution and By-Laws, Walter Varnum, *Chairman*.
5. Report of Resolutions Committee, A. C. Taylor, *Chairman*.
6. Reports of Special Committees.
7. Unfinished business.
8. New Business.
9. Report of Nominating Committee.
10. Election and Installation of Officers.
11. Adjournment.

CONFERENCE OF PHARMACEUTICAL ASSOCIATION SECRETARIES.

The Conference of Pharmaceutical Association Secretaries will devote its time to round table discussion of timely topics. The following subjects have been suggested but the list will undoubtedly be augmented before the opening of the convention:

1. Will State Fair-Trade Acts solve the problem of price stabilization?
2. The importance of State Association Bulletins, and how to handle them.
3. Where geographical conditions permit, should district meetings be held throughout the year?
4. Certain states have the problem of powerful city associations overshadowing the state associations and as a result have poorly attended state conventions; what can be done about it?
5. What can be done to increase the attendance at our conferences?
6. Would it be feasible to build up a manual of fundamentals of secretarial activities?

SOUTH DAKOTA RESOLUTIONS.

Among the resolutions passed at the South Dakota meeting are the following:

The endorsement of a fair trade act for passage at the next session of legislature.

Commendation of the action of the State Board of Pharmacy in recent litigations.

Endorsing the recommendations of President Daniels in their entirety.

Expressing appreciation for the continued support accorded the association by the School of Pharmacy in Brookings.

Recommending the Robinson-Patman Bill and the Tydings Fair Trade Enabling Act.

Reëndorsing the Interprofessional Council and recommending another Interallied Professional meeting to be held in conjunction with the state association convention.

Endorsing the officials of the N. A. R. D. and of the A. PH. A.

Commending the outstanding work done by the prescription pricing committee.

NOTICE TO CONTRIBUTORS TO THE JOURNAL AMERICAN PHARMACEUTICAL ASSOCIATION.

The following notice has been prepared from comments received from members of the Board of Review of Papers and of the Publication Committee.

Manuscripts should be sent to Editor E. G. Eberle, 2215 Constitution Ave., N. W., Washington, D. C.

All manuscripts should be typewritten in double spacing on one side of paper $8^1/_2$ x 11 inches, and should be mailed in a flat package—not rolled. The original (*not* carbon) copy should be sent. The original drawings, not photographs of drawings, should accompany the manuscript. Authors should indicate on the manuscript the approximate position of text figures. All drawings should be marked with the author's name and address.

A condensed title running page headline, not to exceed thirty-five letters, should be given on a separate sheet and placed at the beginning of each article.

The method of stating the laboratory in which the work is done should be uniform and placed as a footnote at end of first page, giving Department, School or College. The date when received for publication should be given.

Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperature (for example: 2 Kg., 1 inch, 20.5 cc., 300° C.). Spell out all indefinite and approximate periods of time and other numerals which are used in a general manner (for example: one hundred years ago, about two and one-half hours, seven times).

Standard abbreviations should be used whenever weights and measures are given in the metric system, *e. g.*, 10 Kg., 2.25 cc., etc. The forms to be used are: cc., Kg., mg., mm., L. and M.

Figures should be numbered from 1 up, beginning with the text-figures (line engravings are always treated as text-figures and should be designed as such) and continuing through the plates. The reduction desired should be clearly indicated on the margin of the drawing. All drawings should be made with India ink, preferably on white tracing paper or cloth. If coördinate paper is used, a blue-lined paper must be chosen. Usually it is desirable to ink in the large squares so that the curves can be more easily read. Lettering should be plain and large enough to reproduce well when the drawing is reduced to the width of a printed page (usually about 4 inches). Photographs intended for half-tone reproduction should be securely mounted with colorless paste.

"Figure" should be spelled out at the beginning of a sentence; elsewhere it is abbreviated to "Fig.;" per cent—2 words.

The expense for a limited number of figures and plates will be borne by the JOURNAL; expense for cuts in excess of this number must be defrayed by the author.

References to the literature cited should be grouped at the end of the manuscript under the *References*. The citations should be numbered consecutively in the order of their appearance (their location in the text should be indicated by full-sized figures included in parentheses). The sequence followed in the citations should be: Author's name (with initials), name of publication, volume number, page number and the date in parentheses. Abbreviations for journals should conform to the style of *Chemical Abstracts*, published by the American Chemical Society.

(1) Author, A. Y., *Am. J. Physiol.*, 79, 289 (1927).

Papers presented at the Sections of the AMERICAN PHARMACEUTICAL ASSOCIATION's annual meeting become the property of the Association and may at the discretion of the Editor be published in the JOURNAL. Papers presented at these Sections may be published in other periodicals only after the release of the papers by the Board of Review of Papers of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The Editor will appreciate comments from Board of Review and Committee on Publication, members, authors and others interested.

Errors in programs, changes and additions will be made in Official Program.